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(54) Title: PROSTATE CANCER EXPRESSION PROFILES

(57) Abstract: The present invention relates to all facets of novel polynucleotides, the polypeptides they encode, antibodies and specific binding partners thereto, and their applications to research, diagnosis, drub discovery, therapy, clinical medicine, forensic science and medicine, etc. The polynucleotides are differentially-regulated in prostate cancer and are therefore useful in variety of ways, including, but not limited to, as molecular markers, as drug targets, and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determining predisposition to, etc., diseases and conditions, to prostate cancer.

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PROSTATE CANCER EXPRESSION PROFILES

This application claims the benefit U.S. Provisional Application No. 60/281,731, filed April 6, 2001, and U.S. Provisional Application No. 60/281,732, filed April 6, 2001, which are hereby incorporated by reference in their entirety.

DESCRIPTION OF THE DRAWINGS

Tables 1 and 2 list genes differentially-regulated in prostate cancer. "DNA SEQ ID" and "Prt SEQ ID" refer to the corresponding DNA and protein sequences in the attached sequence listing. The genes can alternatively be referred to by GenBank accession number in the fifth column ("GI#") or the "identifier" in the third column. The genes listed in Table 1 are up-regulated, and those in Table 2 are down-regulated ("Exp" refers to the expression profile, U is up-regulated expression, and D is down-regulated expression). The characterization of the gene under the "description" heading is based on its listing in GenBank. 5', 3', genomic sequences, etc., which correspond to the genes can be retrieved routinely from Genbank, e.g., by searching the accession number. SEQ ID NOS 1-107 are DNA, and 108-211 are polypeptide. These sequences, and all information referenced to the accession number, are incorporated by reference in their entirety.

The polypeptide sequences was analyzed for the presence of functional domains using the publicly available Pfam program. This information is summarized in Table 3. Domains present in each polypeptide are listed under "domain." Any abbreviations are those used in Pfam. The start of the domain is indicated by "seq-f" and the end of the domain by "seq-t." The "score" is the statistical score of this match to the domain in bits. In general, a higher score indicates a better match. "E" is the statistical score of this match in Evalue (frequentist) approach. The smaller score in this case shows a better match between the domain and the query sequence. For more information on the program and scoring, see, e.g., Sonnhammer et al., *Proteins: Structure, Function and Genetics* 28:405-420 (1997); Sonnhammer et al., *Nucleic Acids Research*, 26:320-322 (1998); Bateman et al., *Nucleic Acids Research*, 27:260-262 (1999); Bateman et al., *Nucleic Acids Research*, 28:263-266 (2000).

DESCRIPTION OF THE INVENTION

The present invention relates to all facets of novel polynucleotides, the polypeptides they encode, antibodies and specific binding partners thereto, and their applications to research, diagnosis, drug discovery, therapy, clinical medicine, forensic science and medicine, etc. The polynucleotides are differentially regulated in prostate cancer and are therefore useful in variety of ways, including, but not limited to, as molecular markers, as drug targets, and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determining predisposition to, etc., diseases and conditions,, especially relating to prostate cancer. The identification of specific genes, and groups of genes, expressed in pathways physiologically relevant to prostate cancer permits the definition of functional and disease pathways, and the delineation of targets in these pathways which are useful in diagnostic, therapeutic, and clinical applications. The present invention also relates to methods of using the polynucleotides and related products (proteins, antibodies, etc.) in business and computer-related methods, e.g., advertising, displaying, offering, selling, etc., such products for sale, commercial use, licensing, etc.

Prostate cancer is the most common form of cancer diagnosed in the American male, occurring predominantly in males over age 50. The number of men diagnosed with prostate cancer has steadily increased as a result of the increasing population of older men. The American Cancer Society estimates that in the year 2000, about 180,000 American men were diagnosed with prostate cancer and about 32,000 died from the disease. In comparison, 1998 estimates for lung cancer in men were 171,500 cases and 160,100 deaths, and for colorectal cancer, the estimates were 131,600 cases and 56,000 deaths. Despite these high numbers, 89 percent of men diagnosed with the disease will survive at least five years and 63 percent will survive at least 10 years.

Patients having prostate cancer display a wide range of phenotypes. In some men, following detection, the tumor remains a latent histological tumor and does not become clinically significant. However, in other men, the tumor progresses rapidly, metastasizing and killing the patient in a relatively short time. Prostate cancer can be cured if the tumor is confined to a small region of the gland and is discovered at early stage. In such cases, radiation or surgical removal often results in complete elimination of the disease. Frequently, however, the prostate cancer has already spread to surrounding tissue and metastasized to

remote locations. In these cases, radiation and other therapies, are less likely to effect a complete cure.

Androgen deprivation is a conventional therapy to treat prostate cancer. Androgen blockade can be achieved through several different routes. Androgen suppressive drugs include, e.g., Lupron (leuprolide acetate), Casodex (bicalutamide), Eulexin (flutamide), Nilandron (nilutamide), Zoladex (goserelin acetate implant), and Viadur (leuprolide acetate), which act through several different mechanisms. While these drugs may offer remission and tumor regression in many cases, often the therapeutic effects are only temporary. Prostate tumors lose their sensitivity to such treatments, and become androgen-independent. Thus, new therapies are clearly needed.

The first clinical symptoms of prostate cancer are typically urinary disturbances, including painful and more frequent urination. Diagnosis for prostate cancer is usually accomplished using a combination of different procedures. Since the prostate is located next to the rectum, rectal digital examination allows the prostate to be examined manually for the presence of hyperplasia and abnormal tissue masses. Usually, this is the first line of detection. If a palpable mass is observed, a blood specimen can be assayed for prostate-specific antigen (PSA). Very little PSA is present in the blood of a healthy individual, but BPH and prostate cancer can cause large amounts of PSA to be released into the blood, indicating the presence of diseased tissue. Definitive diagnosis is generally accomplished by biopsy of the prostate tissue.

No single gene or protein has been identified which is responsible for the etiology of all prostate cancers. Although PSA is widely used as a diagnostic reagent, it has limitations in its sensitivity and its ability to detect early cancers. It is estimated that approximately 20% to 30% of tumors will be missed when PSA is used alone. It is likely that diagnostic and prognostic markers for prostate cancer disease will involve the identification and use of many different genes and gene products to reflect its multifactorial origin.

A continuing goal is to characterize the gene expression patterns of the various prostate cancers to genetically differentiate them, providing important guidance in preventing and treating cancers. Molecular pictures of cancer, such as the pattern of differentially-regulated genes identified herein, provide an important tool for molecularly dissecting and classifying cancer, identifying drug targets, providing prognosis and therapeutic information, etc. For instance, an array of polynucleotides corresponding to genes differentially regulated in prostate cancer can be used to screen tissue samples for the existence of cancer, to

categorize the cancer (e.g., by the particular pattern observed), to grade the cancer (e.g., by the number of differentially-regulated genes and their amounts of expression), to identify the source of a secondary tumor, to screen for metastatic cells, etc. These arrays can be used in combination with other markers, e.g., PSA, PMSA (prostate membrane specific antigen), or any of the grading systems used in clinical medicine.

As indicated by these studies, cancer is a highly diverse disease. Although all cancers share certain characteristics, the underlying cause and disease progression can differ significantly from patient to patient. So far, over a dozen distinct genes have been identified which, when mutant, result in a cancer. In breast cancer, alone, a handful of different genes have been isolated which either cause the cancer, or produce a predisposition to it. As a consequence, disease phenotypes for a particular cancer do not look all the same. In addition to the differences in the gene(s) responsible for the cancer, heterogeneity among individuals, e.g., in age, health, sex, and genetic background, can also influence the disease and its progression. Gene penetrance, in particular, can vary widely among population members. Recent studies have shown tremendous diversity in gene expression patterns among cancer patients. For these and other reasons, one gene/polypeptide target alone can be insufficient to diagnose or treat a cancer. Even a gene which is highly differentially-expressed and penetrant in cancer patients may not be so highly expressed in all patients and at all stages of the cancer. By selecting a set of genes and/or the polypeptides they encode, cancer diagnostics and therapeutics can be designed which effectively diagnose and treat a population of diseased individuals, rather than only a small handful when single genes are targeted.

Nucleic acids

In accordance with the present invention, genes have been identified which are differentially expressed in prostate cancer. Tables 1 and 2 list of genes which are differentially-regulated in the cancer. These genes can be further divided into groups based on additional characteristics of their expression and the tissues in which they are expressed. For instance, genes can be further subdivided based on the stage and/or grade of the cancer in which they are expressed. Genes can also be grouped based on their penetrance in a prostate cancer, e.g., expressed in all prostate cancer examined, expressed in a certain percentage of prostate cancer examined, etc. Additionally, genes can be categorized by their function and/or the polypeptides they encode. This includes, but is not limited to, cellular

localization, functional activity (e.g., kinase, cytoskeletal element, or transcriptional factor), functional pathway (e.g., protein manufacture, cell signaling, cell movement, cell adhesion, responsivity to cAMP, energy production, etc.), etc. These groupings do not restrict or limit the use such genes in therapeutic, diagnostic, prognostic, etc., applications. For instance, a gene which is expressed in only some cancers (e.g., incompletely penetrant) may be useful in therapeutic applications to treat a subset of cancers. Similarly, a co-penetrant gene, or a gene which is expressed in prostate cancer and other normal tissues, may be useful as a therapeutic or diagnostic, even if its expression pattern is not highly prostate specific. Thus, the uses of the genes or their products are not limited by their patterns of expression.

For genes which are differentially-regulated, gene and protein replacement therapies can be used therapeutically to restore expression levels to normal. When a protein product is to be administered, secreted proteins are more likely to be targets for replacement therapy than intracellular and membrane-bound proteins. For the latter classes, gene therapy may be a more effective means of delivery, e.g., administering a gene which is expressed inside a cell on or on its surface.

By the phrase "differential expression," it is meant that the levels of expression of a gene, as measured by its transcription or translation product, are different depending upon the specific cell-type or tissue (e.g., in an averaging assay that looks at a population of cells). There are no absolute amounts by which the gene expression levels must vary, as long as the differences are measurable.

The phrase "down-regulated" indicates that an mRNA transcript or other nucleic acid corresponding to a polynucleotide of the present invention is expressed in lower amounts in a cancer as compared to the same transcript expressed in normal cells from which the cancer was derived. In general, down-regulation can be assessed by any suitable method, including any of the nucleic acid detection and hybridization methods mentioned below, as well as polypeptide-based methods. Down-regulation also includes going from substantially no expression in a normal tissue, from detectable expression in a normal tissue, from significant expression in a normal tissue, to higher levels in the cancer.

The phrase "up-regulated" indicates that an mRNA transcript or other nucleic acid corresponding to a polynucleotide of the present invention is expressed in larger amounts in a cancer as compared to the same transcript expressed in normal cells from which the cancer was derived. For instance, a gene's up-regulation can be determined by comparing its abundance per gram of RNA (e.g., total RNA, polyadenylated mRNA, etc.) extracted from a

cancer tissue in comparison to the corresponding normal tissue. The normal tissue can be from the same or different individual or source. For convenience, it can be supplied as a separate component or in a kit in combination with probes and other reagents for detecting genes. The quantity by which a nucleic acid is up-regulated can be any value, e.g., more than 10%, 50%, 2-fold, 5-fold, 10-fold, etc. Up-regulation also includes going from substantially no expression, to detectable expression, to significant or highly restricted expression, etc.

Differential regulation can be determined by any suitable method, e.g., by comparing its abundance per gram of RNA (e.g., total RNA, polyadenylated mRNA, etc.) extracted from a prostate tissue in comparison to the corresponding normal tissue. The normal tissue can be from the same or different individual or source. For convenience, it can be supplied as a separate component or in a kit in combination with probes and other reagents for detecting genes. The quantity by which a nucleic acid is differentially-regulated can be any value, e.g., about 10% more or less of normal expression, about 50% more or less of normal expression, 2-fold more or less, 5-fold more or less, 10-fold more or less, etc.

The amount of transcript can also be compared to a different gene in the same sample, especially a gene whose abundance is known and substantially no different in its expression between normal and cancer cells (e.g., a "control" gene). If represented as a ratio, with the quantity of differentially-regulated gene transcript in the numerator and the control gene transcript in the denominator, the ratio would be larger, e.g., in breast cancer than in a sample from normal breast tissue.

Differential-regulation can arise through a number of different mechanisms. The present invention is not bound by any specific way through which it occurs. Differential-regulation of a polynucleotide can occur, e.g., by modulating (1) transcriptional rate of the gene (e.g., increasing its rate, inducing or stimulating its transcription from a basal, low-level rate, etc.), (2) the post-transcriptional processing of RNA transcripts, (3) the transport of RNA from the nucleus into the cytoplasm, (4) RNA nuclear and cytoplasmic turnover and polypeptide turnover (e.g., by virtue of having higher stability or resistance to degradation), and combinations thereof. See, e.g., Tollervey and Caceras, *Cell*, 103:703-709, 2000.

A differentially-regulated polynucleotide is useful in a variety of different applications as described in greater details below. Because it is more abundant in cancer, it and its expression products can be used in a diagnostic test to assay for the presence of cancer, e.g., in tissue sections, in a biopsy sample, in total RNA, in lymph, in blood, etc. Differentially-regulated polynucleotides and polypeptides can be used individually, or in

groups, to assess the cancer, e.g., to determine the specific type of cancer, its stage of development, the nature of the genetic defect, etc., or to assess the efficacy of a treatment modality. How to use polynucleotides in diagnostic and prognostic assays is discussed below. In addition, the polynucleotides and the polypeptides they encode, can serve as a target for therapy or drug discovery. A polypeptide, coded for by a differentially-regulated polynucleotide, which is displayed on the cell-surface, can be a target for immunotherapy to destroy, inhibit, etc., the diseased tissue. Differentially-regulated transcripts can also be used in drug discovery schemes to identify pharmacological agents which suppress, inhibit, etc., their differential-regulation, thereby preventing the phenotype associated with their expression. Thus, a differentially-regulated polynucleotide and its expression products of the present invention have significant applications in diagnostic, therapeutic, prognostic, drug development, and related areas.

The expression patterns of the differentially expressed genes disclosed herein can be described as a "fingerprint" in that they are a distinctive pattern displayed by a cancer. Just as with a fingerprint, an expression pattern can be used as a unique identifier to characterize the status of a tissue sample. The list of genes represented in Tables 1 and 2 provide an example of a cell expression profile for a prostate cancer. It can be used as a point of reference to compare and characterize unknown samples and samples for which further information is sought. Tissue fingerprints can be used in many ways, e.g., to classify an unknown tissue as being a prostate cancer, to determine the origin of a particular cancer (e.g., the origin of metastatic cells), to determine the presence of a cancer in a biopsy sample, to assess the efficacy of a cancer therapy in a human patient or a non-human animal model, to detect circulating cancer cells in blood or a lymph node biopsy, etc. While the expression profile of the complete gene set represented in Tables 1 and 2 may be most informative, a fingerprint containing expression information from less than the full collection can be useful, as well. In the same way that an incomplete fingerprint may contain enough of the pattern of whorls, arches, loops, and ridges, to identify the individual, a cell expression fingerprint containing less than the full complement may be adequate to provide useful and unique identifying and other information about the sample. Moreover, cancer is a multifactorial disease, involving genetic aberrations in more than gene locus. This multifaceted nature may be reflected in different cell expression profiles associated with breast cancers arising in different individuals, in different locations in the same individual, or even within the same cancer locus. As a result, a complete match with a particular cell expression profile, as

shown herein, is not necessary to classify a cancer as being of the same type or stage. Similarity to one cell expression profile, e.g., as compared to another, can be adequate to classify cancer types, grades, and stages. SEQ ID NOS 1-211 are referred to generally as "genes" to indicate that they represent specific gene loci, and are not limited to the particular nucleotide and polypeptide sequences disclosed herein. For example, fibronectin (SEQ ID NO 60 and 196) is up-regulated in prostate cancers. Probes to detect its up regulation can be selected from the attached specific sequences, as well as genomic, upstream, downstream, and intron sequences which are not in the attached sequence listing.

A mammalian polynucleotide, or fragment thereof, of the present invention is a polynucleotide having a nucleotide sequence obtainable from a natural source. It therefore includes naturally-occurring normal, naturally-occurring mutant, and naturally-occurring polymorphic alleles (e.g., SNPs), differentially-spliced transcripts, splice-variants, etc. By the term "naturally-occurring," it is meant that the polynucleotide is obtainable from a natural source, e.g., animal tissue and cells, body fluids, tissue culture cells, forensic samples. Natural sources include, e.g., living cells obtained from tissues and whole organisms, tumors, cultured cell lines, including primary and immortalized cell lines. Naturally-occurring mutations can include deletions (e.g., a truncated amino- or carboxy-terminus), substitutions, inversions, or additions of nucleotide sequence. These genes can be detected and isolated by polynucleotide hybridization according to methods which one skilled in the art would know, e.g., as discussed below.

A polynucleotide according to the present invention can be obtained from a variety of different sources. It can be obtained from DNA or RNA, such as polyadenylated mRNA or total RNA, e.g., isolated from tissues, cells, or whole organism. The polynucleotide can be obtained directly from DNA or RNA, from a cDNA library, from a genomic library, etc. The polynucleotide can be obtained from a cell or tissue (e.g., from an embryonic or adult tissues) at a particular stage of development, having a desired genotype, phenotype, disease status, etc.

The genes described in Tables 1 and 2 can be partial sequences that correspond to full-length, naturally-occurring transcripts. The present invention includes, as well, full-length polynucleotides that comprise these partial sequences, e.g., genomic DNAs and polynucleotides comprising a start and stop codon, a start codon and a polyA tail, a transcription start and a polyA tail, etc. These sequences can be obtained by any suitable method, e.g., using a partial sequence as a probe to select a full-length cDNA from a library

containing full-length inserts. A polynucleotide which "codes without interruption" refers to a polynucleotide having a continuous open reading frame ("ORF") as compared to an ORF which is interrupted by introns or other noncoding sequences.

Genomic

The present invention also relates genomic DNA from which the polynucleotides of the present invention can be derived. A genomic DNA coding for a human, mouse, or other mammalian polynucleotide, can be obtained routinely, for example, by screening a genomic library (e.g., a YAC library) with a polynucleotide of the present invention, or by searching nucleotide databases, such as GenBank and EMBL, for matches. Promoter and other regulatory regions can be identified upstream of coding and expressed RNAs, and assayed routinely for activity, e.g., by joining to a reporter gene (e.g., CAT, GFP, alkaline phosphatase, luciferase, galatosidase). A promoter obtained from a prostate selective gene can be used, e.g., in gene therapy to obtain tissue-specific expression of a heterologous gene (e.g., coding for a therapeutic product or cytotoxin).

Constructs

A polynucleotide of the present invention can comprise additional polynucleotide sequences, e.g., sequences to enhance expression, detection, uptake, cataloging, tagging, etc. A polynucleotide can include only coding sequence; a coding sequence and additional non-naturally occurring or heterologous coding sequence (e.g., sequences coding for leader, signal, secretory, targeting, enzymatic, fluorescent, antibiotic resistance, and other functional or diagnostic peptides); coding sequences and non-coding sequences, e.g., untranslated sequences at either a 5' or 3' end, or dispersed in the coding sequence, e.g., introns.

A polynucleotide according to the present invention also can comprise an expression control sequence operably linked to a polynucleotide as described above. The phrase "expression control sequence" means a polynucleotide sequence that regulates expression of a polypeptide coded for by a polynucleotide to which it is functionally ("operably") linked. Expression can be regulated at the level of the mRNA or polypeptide. Thus, the expression control sequence includes mRNA-related elements and protein-related elements. Such elements include promoters, enhancers (viral or cellular), ribosome binding sequences, transcriptional terminators, etc. An expression control sequence is operably linked to a nucleotide coding sequence when the expression control sequence is positioned in such a

manner to effect or achieve expression of the coding sequence. For example, when a promoter is operably linked 5' to a coding sequence, expression of the coding sequence is driven by the promoter. Expression control sequences can include an initiation codon and additional nucleotides to place a partial nucleotide sequence of the present invention in-frame in order to produce a polypeptide (e.g., pET vectors from Promega have been designed to permit a molecule to be inserted into all three reading frames to identify the one that results in polypeptide expression). Expression control sequences can be heterologous or endogenous to the normal gene.

A polynucleotide of the present invention can also comprise nucleic acid vector sequences, e.g., for cloning, expression, amplification, selection, etc. Any effective vector can be used. A vector is, e.g., a polynucleotide molecule which can replicate autonomously in a host cell, e.g., containing an origin of replication. Vectors can be useful to perform manipulations, to propagate, and/or obtain large quantities of the recombinant molecule in a desired host. A skilled worker can select a vector depending on the purpose desired, e.g., to propagate the recombinant molecule in bacteria, yeast, insect, or mammalian cells. The following vectors are provided by way of example. Bacterial: pQE70, pQE60, pQE-9 (Qiagen), pBS, pD10, Phagescript, phiX174, pBK Phagemid, pNH8A, pNH16a, pNH18Z, pNH46A (Stratagene); Bluescript KS+II (Stratagene); ptrc99a, pKK223-3, pKK233-3, pDR54 0, pRIT5 (Pharmacia). Eukaryotic: PWLNEO, pSV2CAT, pOG44, pXT1, pSG (Stratagene), pSVK3, PBPV, PMSG, pSVL (Pharmacia), pCR2.1/TOPO, pCRII/TOPO, pCR4/TOPO, pTrcHisB, pCMV6-XL4, etc. However, any other vector, e.g., plasmids, viruses, or parts thereof, may be used as long as they are replicable and viable in the desired host. The vector can also comprise sequences which enable it to replicate in the host whose genome is to be modified.

Hybridization

Polynucleotide hybridization, as discussed in more detail below, is useful in a variety of applications, including, in gene detection methods, for identifying mutations, for making mutations, to identify homologs in the same and different species, to identify related members of the same gene family, in diagnostic and prognostic assays, in therapeutic applications (e.g., where an antisense polynucleotide is used to inhibit expression), etc.

The ability of two single-stranded polynucleotide preparations to hybridize together is a measure of their nucleotide sequence complementarity, e.g., base-pairing between nucleotides, such as A-T, G-C, etc. The invention thus also relates to polynucleotides, and their complements, which hybridize to a polynucleotide comprising a nucleotide sequence as set forth in Tables 1 and 2 and genomic sequences thereof. A nucleotide sequence hybridizing to the latter sequence will have a complementary polynucleotide strand, or act as a template for one in the presence of a polymerase (i.e., an appropriate polynucleotide synthesizing enzyme). The present invention includes both strands of polynucleotide, e.g., a sense strand and an anti-sense strand.

Hybridization conditions can be chosen to select polynucleotides which have a desired amount of nucleotide complementarity with the nucleotide sequences set forth in Tables 1 and 2 and genomic sequences thereof. A polynucleotide capable of hybridizing to such sequence, preferably, possesses, e.g., about 70%, 75%, 80%, 85%, 87%, 90%, 92%, 95%, 97%, 99%, or 100% complementarity, between the sequences. The present invention particularly relates to polynucleotide sequences which hybridize to the nucleotide sequences set forth in Tables 1 and 2 or genomic sequences thereof, under low or high stringency conditions. These conditions can be used, e.g., to select corresponding homologs in non-human species.

Polynucleotides which hybridize to polynucleotides of the present invention can be selected in various ways. Filter-type blots (i.e., matrices containing polynucleotide, such as nitrocellulose), glass chips, and other matrices and substrates comprising polynucleotides (short or long) of interest, can be incubated in a prehybridization solution (e.g., 6X SSC, 0.5% SDS, 100 µg/ml denatured salmon sperm DNA, 5X Denhardt's solution, and 50% formamide), at 22-68°C, overnight, and then hybridized with a detectable polynucleotide probe under conditions appropriate to achieve the desired stringency. In general, when high homology or sequence identity is desired, a high temperature can be used (e.g., 65 °C). As the homology drops, lower washing temperatures are used. For salt concentrations, the lower the salt concentration, the higher the stringency. The length of the probe is another consideration. Very short probes (e.g., less than 100 base pairs) are washed at lower temperatures, even if the homology is high. With short probes, formamide can be omitted. See, e.g., *Current Protocols in Molecular Biology*, Chapter 6, Screening of Recombinant Libraries; Sambrook et al., *Molecular Cloning*, 1989, Chapter 9.

For instance, high stringency conditions can be achieved by incubating the blot overnight (e.g., at least 12 hours) with a long polynucleotide probe in a hybridization solution containing, e.g., about 5X SSC, 0.5% SDS, 100 µg/ml denatured salmon sperm DNA and 50% formamide, at 42°C. Blots can be washed at high stringency conditions that allow, e.g., for less than 5% bp mismatch (e.g., wash twice in 0.1% SSC and 0.1% SDS for 30 min at 65°C), i.e., selecting sequences having 95% or greater sequence identity.

Other non-limiting examples of high stringency conditions includes a final wash at 65°C in aqueous buffer containing 30 mM NaCl and 0.5% SDS. Another example of high stringent conditions is hybridization in 7% SDS, 0.5 M $NaPO_4$, pH 7, 1 mM EDTA at 50°C, e.g., overnight, followed by one or more washes with a 1% SDS solution at 42°C. Whereas high stringency washes can allow for less than 5% mismatch, reduced or low stringency conditions can permit up to 20% nucleotide mismatch. Hybridization at low stringency can be accomplished as above, but using lower formamide conditions, lower temperatures and/or lower salt concentrations, as well as longer periods of incubation time.

Hybridization can also be based on a calculation of melting temperature (Tm) of the hybrid formed between the probe and its target, as described in Sambrook et al.. Generally, the temperature Tm at which a short oligonucleotide (containing 18 nucleotides or fewer) will melt from its target sequence is given by the following equation: Tm = (number of A's and T's) x 2°C + (number of C's and G's) x 4°C. For longer molecules, $Tm = 81.5 + 16.6 \log_{10}[Na^+] + 0.41(\%GC) - 600/N$ where $[Na^+]$ is the molar concentration of sodium ions, %GC is the percentage of GC base pairs in the probe, and N is the length. Hybridization can be carried out at several degrees below this temperature to ensure that the probe and target can hybridize. Mismatches can be allowed for by lowering the temperature even further.

Stringent conditions can be selected to isolate sequences, and their complements, which have, e.g., at least about 90%, 95%, or 97%, nucleotide complementarity between the probe (e.g., a short polynucleotide of Tables 1 and 2 or genomic sequences thereof) and a target polynucleotide.

Other homologs of polynucleotides of the present invention can be obtained from mammalian and non-mammalian sources according to various methods. For example, hybridization with a polynucleotide can be employed to select homologs, e.g., as described in Sambrook et al., *Molecular Cloning*, Chapter 11, 1989. Such homologs can have varying amounts of nucleotide and amino acid sequence identity and similarity to such

polynucleotides of the present invention. Mammalian organisms include, e.g., mice, rats, monkeys, pigs, cows, etc. Non-mammalian organisms include, e.g., vertebrates, invertebrates, zebra fish, chicken, Drosophila, C. elegans, Xenopus, yeast such as S. pombe, S. cerevisiae, roundworms, prokaryotes, plants, Arabidopsis, artemia, viruses, etc. The degree of nucleotide sequence identity between human and mouse can be about, e.g. 70% or more, 85% or more for open reading frames, etc.

Alignment

Alignments can be accomplished by using any effective algorithm. For pairwise alignments of DNA sequences, the methods described by Wilbur-Lipman (e.g., Wilbur and Lipman, *Proc. Natl. Acad. Sci.*, 80:726-730, 1983) or Martinez/Needleman-Wunsch (e.g., Martinez, *Nucleic Acid Res.*, 11:4629-4634, 1983) can be used. For instance, if the Martinez/Needleman-Wunsch DNA alignment is applied, the minimum match can be set at 9, gap penalty at 1.10, and gap length penalty at 0.33. The results can be calculated as a similarity index, equal to the sum of the matching residues divided by the sum of all residues and gap characters, and then multiplied by 100 to express as a percent. Similarity index for related genes at the nucleotide level in accordance with the present invention can be greater than 70%, 80%, 85%, 90%, 95%, 99%, or more. Pairs of protein sequences can be aligned by the Lipman-Pearson method (e.g., Lipman and Pearson, *Science*, 227:1435-1441, 1985) with k-tuple set at 2, gap penalty set at 4, and gap length penalty set at 12. Results can be expressed as percent similarity index, where related genes at the amino acid level in accordance with the present invention can be greater than 65%, 70%, 75%, 80%, 85%, 90%, 95%, 99%, or more. Various commercial and free sources of alignment programs are available, e.g., MegAlign by DNA Star, BLAST (National Center for Biotechnology Information), BCM (Baylor College of Medicine) Launcher, etc.

Percent sequence identity can also be determined by other conventional methods, e.g., as described in Altschul et al., *Bull. Math. Bio.* 48: 603-616, 1986 and Henikoff and Henikoff, *Proc. Natl. Acad. Sci.* USA 89:10915-10919, 1992.

Specific polynucleotide probes

A polynucleotide of the present invention can comprise any continuous nucleotide sequence of Tables 1 and 2, sequences which share sequence identity thereto, or complements thereof. The term "probe" refers to any substance that can be used to detect,

identify, isolate, etc., another substance. A polynucleotide probe is comprised of nucleic acid can be used to detect, identify, etc., other nucleic acids, such as DNA and RNA.

These polynucleotides can be of any desired size that is effective to achieve the specificity desired. For example, a probe can be from about 7 or 8 nucleotides to several thousand nucleotides, depending upon its use and purpose. For instance, a probe used as a primer PCR can be shorter than a probe used in an ordered array of polynucleotide probes. Probe sizes vary, and the invention is not limited in any way by their size, e.g., probes can be from about 7-2000 nucleotides, 7-1000, 8-700, 8-600, 8-500, 8-400, 8-300, 8-150, 8-100, 8-75, 7-50, 10-25, 14-16, at least about 8, at least about 10, at least about 15, at least about 25, etc. The polynucleotides can have non-naturally-occurring nucleotides, e.g., inosine, AZT, 3TC, etc. The polynucleotides can have 100% sequence identity or complementarity to a sequence of Tables 1 and 2, or it can have mismatches or nucleotide substitutions, e.g., 1, 2, 3, 4, or 5 substitutions. The probes can be single-stranded or double-stranded.

In accordance with the present invention, a polynucleotide can be present in a kit, where the kit includes, e.g., one or more polynucleotides, a desired buffer (e.g., phosphate, tris, etc.), detection compositions, RNA or cDNA from different tissues to be used as controls, libraries, etc. The polynucleotide can be labeled or unlabeled, with radioactive or non-radioactive labels as known in the art. Kits can comprise one or more pairs of polynucleotides for amplifying nucleic acids specific for differentially-regulated genes of the present invention, e.g., comprising a forward and reverse primer effective in PCR. These include both sense and anti-sense orientations. For instance, in PCR-based methods (such as RT-PCR), a pair of primers are typically used, one having a sense sequence and the other having an antisense sequence.

Another aspect of the present invention is a nucleotide sequence that is specific to, or for, a selective polynucleotide. The phrases "specific for" or "specific to" a polynucleotide have a functional meaning that the polynucleotide can be used to identify the presence of one or more target genes in a sample. It is specific in the sense that it can be used to detect polynucleotides above background noise ("non-specific binding"). A specific sequence is a defined order of nucleotides which occurs in the polynucleotide, e.g., in the nucleotide sequences of Tables 1 and 2. A probe or mixture of probes can comprise a sequence or sequences that are specific to a plurality of target sequences, e.g., where the sequence is a consensus sequence, a functional domain, etc., e.g., capable of recognizing a family of related genes. Such sequences can be used as probes in any of the methods described herein or

incorporated by reference. Both sense and antisense nucleotide sequences are included. A specific polynucleotide according to the present invention can be determined routinely.

A polynucleotide comprising a specific sequence can be used as a hybridization probe to identify the presence of, e.g., human or mouse polynucleotide, in a sample comprising a mixture of polynucleotides, e.g., on a Northern blot. Hybridization can be performed under high stringent conditions (see, above) to select polynucleotides (and their complements which can contain the coding sequence) having at least 90%, 95%, 99%, etc., identity (i.e., complementarity) to the probe, but less stringent conditions can also be used. A specific polynucleotide sequence can also be fused in-frame, at either its 5' or 3' end, to various nucleotide sequences as mentioned throughout the patent, including coding sequences for enzymes, detectable markers, GFP, etc, expression control sequences, etc.

A polynucleotide probe, especially one that is specific to a polynucleotide of the present invention, can be used in gene detection and hybridization methods as already described. In one embodiment, a specific polynucleotide probe can be used to detect whether a particular tissue or cell-type is present in a target sample. To carry out such a method, a selective polynucleotide can be chosen which is characteristic of the desired target tissue. Such polynucleotide is preferably chosen so that it is expressed or displayed in the target tissue, but not in other tissues which are present in the sample. For instance, if detection of prostate is desired, it may not matter whether the selective polynucleotide is expressed in other tissues, as long as it is not expressed in cells normally present in blood, e.g., peripheral blood mononuclear cells. Starting from the selective polynucleotide, a specific polynucleotide probe can be designed which hybridizes (if hybridization is the basis of the assay) under the hybridization conditions to the selective polynucleotide, whereby the presence of the selective polynucleotide can be determined.

Probes which are specific for polynucleotides of the present invention can also be prepared using involve transcription-based systems, e.g., incorporating an RNA polymerase promoter into a selective polynucleotide of the present invention, and then transcribing anti-sense RNA using the polynucleotide as a template. See, e.g., U.S. Pat. No. 5,545,522.

Polynucleotide composition

A polynucleotide according to the present invention can comprise, e.g., DNA, RNA, synthetic polynucleotide, peptide polynucleotide, modified nucleotides, dsDNA, ssDNA, ssRNA, dsRNA, and mixtures thereof. A polynucleotide can be single- or double-stranded,

triplex, DNA:RNA, duplexes, comprise hairpins, and other secondary structures, etc. Nucleotides comprising a polynucleotide can be joined via various known linkages, e.g., ester, sulfamate, sulfamide, phosphorothioate, phosphoramidate, methylphosphonate, carbamate, etc., depending on the desired purpose, e.g., resistance to nucleases, such as RNAse H, improved in vivo stability, etc. See, e.g., U.S. Pat. No. 5,378,825. Any desired nucleotide or nucleotide analog can be incorporated, e.g., 6-mercaptoguanine, 8-oxo-guanine, etc.

Various modifications can be made to the polynucleotides, such as attaching detectable markers (avidin, biotin, radioactive elements, fluorescent tags and dyes, energy transfer labels, energy-emitting labels, binding partners, etc.) or moieties which improve hybridization, detection, and/or stability. The polynucleotides can also be attached to solid supports, e.g., nitrocellulose, magnetic or paramagnetic microspheres (e.g., as described in U.S. Pat. No. 5,411,863; U.S. Pat. No. 5,543,289; for instance, comprising ferromagnetic, supermagnetic, paramagnetic, superparamagnetic, iron oxide and polysaccharide), nylon, agarose, diazotized cellulose, latex solid microspheres, polyacrylamides, etc., according to a desired method. See, e.g., U.S. Pat. Nos. 5,470,967, 5,476,925, and 5,478,893.

Polynucleotide according to the present invention can be labeled according to any desired method. The polynucleotide can be labeled using radioactive tracers such as ^{32}P, ^{35}S, ^{3}H, or ^{14}C, to mention some commonly used tracers. The radioactive labeling can be carried out according to any method, such as, for example, terminal labeling at the 3' or 5' end using a radiolabeled nucleotide, polynucleotide kinase (with or without dephosphorylation with a phosphatase) or a ligase (depending on the end to be labeled). A non-radioactive labeling can also be used, combining a polynucleotide of the present invention with residues having immunological properties (antigens, haptens), a specific affinity for certain reagents (ligands), properties enabling detectable enzyme reactions to be completed (enzymes or coenzymes, enzyme substrates, or other substances involved in an enzymatic reaction), or characteristic physical properties, such as fluorescence or the emission or absorption of light at a desired wavelength, etc.

Nucleic acid detection methods

Another aspect of the present invention relates to methods and processes for detecting differentially-regulated genes of the present invention. Detection methods have a variety of applications, including for diagnostic, prognostic, forensic, and research applications. To

accomplish gene detection, a polynucleotide in accordance with the present invention can be used as a "probe." The term "probe" or "polynucleotide probe" has its customary meaning in the art, e.g., a polynucleotide which is effective to identify (e.g., by hybridization), when used in an appropriate process, the presence of a target polynucleotide to which it is designed. Identification can involve simply determining presence or absence, or it can be quantitative, e.g., in assessing amounts of a gene or gene transcript present in a sample. Probes can be useful in a variety of ways, such as for diagnostic purposes, to identify homologs, and to detect, quantitate, or isolate a polynucleotide of the present invention in a test sample.

Assays can be utilized which permit quantification and/or presence/absence detection of a target nucleic acid in a sample. Assays can be performed at the single-cell level, or in a sample comprising many cells, where the assay is "averaging" expression over the entire collection of cells and tissue present in the sample. Any suitable assay format can be used, including, but not limited to, e.g., Southern blot analysis, Northern blot analysis, polymerase chain reaction ("PCR") (e.g., Saiki et al., *Science*, 241:53, 1988; U.S. Pat. Nos. 4,683,195, 4,683,202, and 6,040,166; *PCR Protocols: A Guide to Methods and Applications*, Innis et al., eds., Academic Press, New York, 1990), reverse transcriptase polymerase chain reaction ("RT-PCR"), anchored PCR, rapid amplification of cDNA ends ("RACE") (e.g., Schaefer in *Gene Cloning and Analysis: Current Innovations*, Pages 99-115, 1997), ligase chain reaction ("LCR") (EP 320 308), one-sided PCR (Ohara et al., *Proc. Natl. Acad. Sci.*, 86:5673-5677, 1989), indexing methods (e.g., U.S. Pat. No. 5,508,169), *in situ* hybridization, differential display (e.g., Liang et al., *Nucl. Acid. Res.*, 21:3269-3275, 1993; U.S. Pat. Nos. 5,262,311, 5,599,672 and 5,965,409; WO97/18454; Prashar and Weissman, *Proc. Natl. Acad. Sci.*, 93:659-663, and U.S. Pat. Nos. 6,010,850 and 5,712,126; Welsh et al., *Nucleic Acid Res.*, 20:4965-4970, 1992, and U.S. Pat. No. 5,487,985) and other RNA fingerprinting techniques, nucleic acid sequence based amplification ("NASBA") and other transcription based amplification systems (e.g., U.S. Pat. Nos. 5,409,818 and 5,554,527; WO 88/10315), polynucleotide arrays (e.g., U.S. Pat. Nos. 5,143,854, 5,424,186; 5,700,637, 5,874,219, and 6,054,270; PCT WO 92/10092; PCT WO 90/15070), Qbeta Replicase (PCT/US87/00880), Strand Displacement Amplification ("SDA"), Repair Chain Reaction ("RCR"), nuclease protection assays, subtraction-based methods, Rapid-Scan™, etc. Additional useful methods include, but are not limited to, e.g., template-based amplification methods, competitive PCR (e.g., U.S. Pat. No. 5,747,251), redox-based assays (e.g., U.S. Pat. No. 5,871,918), Taqman-based assays (e.g., Holland et al., *Proc. Natl. Acad. Sci.*, 88:7276-7280, 1991; U.S. Pat. Nos.

5,210,015 and 5,994,063), real-time fluorescence-based monitoring (e.g., U.S. Pat. 5,928,907), molecular energy transfer labels (e.g., U.S. Pat. Nos. 5,348,853, 5,532,129, 5,565,322, 6,030,787, and 6,117,635; Tyagi and Kramer, *Nature Biotech.*, 14:303-309, 1996). Any method suitable for single cell analysis of gene or protein expression can be used, including in situ hybridization, immunocytochemistry, MACS, FACS, flow cytometry, etc. For single cell assays, expression products can be measured using antibodies, PCR, or other types of nucleic acid amplification (e.g., Brady et al., *Methods Mol. & Cell. Biol.* 2, 17-25, 1990; Eberwine et al., 1992, *Proc. Natl. Acad. Sci.*, 89, 3010-3014, 1992; U.S. Pat. No. 5,723,290). These and other methods can be carried out conventionally, e.g., as described in the mentioned publications.

Many of such methods may require that the polynucleotide is labeled, or comprises a particular nucleotide type useful for detection. The present invention includes such modified polynucleotides that are necessary to carry out such methods. Thus, polynucleotides can be DNA, RNA, DNA:RNA hybrids, PNA, etc., and can comprise any modification or substituent which is effective to achieve detection.

Detection can be desirable for a variety of different purposes, including research, diagnostic, prognostic, and forensic. For diagnostic purposes, it may be desirable to identify the presence or quantity of a polynucleotide sequence in a sample, where the sample is obtained from tissue, cells, body fluids, etc. In a preferred method as described in more detail below, the present invention relates to a method of detecting a polynucleotide comprising, contacting a target polynucleotide in a test sample with a polynucleotide probe under conditions effective to achieve hybridization between the target and probe; and detecting hybridization.

Any test sample in which it is desired to identify a polynucleotide or polypeptide thereof can be used, including, e.g., blood, urine, saliva, stool (for extracting nucleic acid, see, e.g., U.S. Pat. No. 6,177,251), swabs comprising tissue, biopsied tissue, tissue sections, cultured cells, etc.

Detection can be accomplished in combination with polynucleotide probes for other genes, e.g., genes which are expressed in other disease states, tissues, cells, such as brain, heart, kidney, spleen, thymus, liver, stomach, small intestine, colon, muscle, lung, testis, placenta, pituitary, thyroid, skin, adrenal gland, pancreas, salivary gland, uterus, ovary, prostate gland, peripheral blood cells (T-cells, lymphocytes, etc.), embryo, normal breast fat,

adult and embryonic stem cells, specific cell-types, such as endothelial, epithelial, myocytes, adipose, luminal epithelial, basoepithelial, myoepithelial, stromal cells, etc.

Polynucleotides can be used in wide range of methods and compositions, including for detecting, diagnosing, staging, grading, assessing, prognosticating, etc. diseases and disorders associated with differentially-regulated genes of the present invention, for monitoring or assessing therapeutic and/or preventative measures, in ordered arrays, etc. Any method of detecting genes and polynucleotides of Tables 1 and 2 can be used; certainly, the present invention is not to be limited how such methods are implemented.

Along these lines, the present invention relates to methods of detecting differentially-regulated genes described herein in a sample comprising nucleic acid. Such methods can comprise one or more the following steps in any effective order, e.g., contacting said sample with a polynucleotide probe under conditions effective for said probe to hybridize specifically to nucleic acid in said sample, and detecting the presence or absence of probe hybridized to nucleic acid in said sample, wherein said probe is a polynucleotide which is Tables 1 and 2, a polynucleotide having, e.g., about 70%, 80%, 85%, 90%, 95%, 99%, or more sequence identity thereto, effective or specific fragments thereof, or complements thereto. The detection method can be applied to any sample, e.g., cultured primary, secondary, or established cell lines, tissue biopsy, blood, urine, stool, and other bodily fluids, for any purpose.

Contacting the sample with probe can be carried out by any effective means in any effective environment. It can be accomplished in a solid, liquid, frozen, gaseous, amorphous, solidified, coagulated, colloid, etc., mixtures thereof, matrix. For instance, a probe in an aqueous medium can be contacted with a sample which is also in an aqueous medium, or which is affixed to a solid matrix, or vice-versa.

Generally, as used throughout the specification, the term "effective conditions" means, e.g., the particular milieu in which the desired effect is achieved. Such a milieu, includes, e.g., appropriate buffers, oxidizing agents, reducing agents, pH, co-factors, temperature, ion concentrations, suitable age and/or stage of cell (such as, in particular part of the cell cycle, or at a particular stage where particular genes are being expressed) where cells are being used, culture conditions (including substrate, oxygen, carbon dioxide, etc.). When hybridization is the chosen means of achieving detection, the probe and sample can be combined such that the resulting conditions are functional for said probe to hybridize specifically to nucleic acid in said sample.

The phrase "hybridize specifically" indicates that the hybridization between single-stranded polynucleotides is based on nucleotide sequence complementarity. The effective conditions are selected such that the probe hybridizes to a preselected and/or definite target nucleic acid in the sample. For instance, if detection of a gene set forth in Tables 1 and 2 is desired, a probe can be selected which can hybridize to such target gene under high stringent conditions, without significant hybridization to other genes in the sample. To detect homologs of a gene set forth in Tables 1 and 2, the effective hybridization conditions can be less stringent, and/or the probe can comprise codon degeneracy, such that a homolog is detected in the sample.

As already mentioned, the methods can be carried out by any effective process, e.g., by Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, *in situ* hybridization, etc., as indicated above. When PCR based techniques are used, two or more probes are generally used. One probe can be specific for a defined sequence which is characteristic of a selective polynucleotide, but the other probe can be specific for the selective polynucleotide, or specific for a more general sequence, e.g., a sequence such as polyA which is characteristic of mRNA, a sequence which is specific for a promoter, ribosome binding site, or other transcriptional features, a consensus sequence (e.g., representing a functional domain). For the former aspects, 5' and 3' probes (e.g., polyA, Kozak, etc.) are preferred which are capable of specifically hybridizing to the ends of transcripts. When PCR is utilized, the probes can also be referred to as "primers" in that they can prime a DNA polymerase reaction.

In addition to testing for the presence or absence of polynucleotides, the present invention also relates to determining the amounts at which polynucleotides of the present invention are expressed in sample and determining the differential expression of such polynucleotides in samples.. Such methods can involve substantially the same steps as described above for presence/absence detection, e.g., contacting with probe, hybridizing, and detecting hybridized probe, but using more quantitative methods and/or comparisons to standards.

The amount of hybridization between the probe and target can be determined by any suitable methods, e.g., PCR, RT-PCR, RACE PCR, Northern blot, polynucleotide microarrays, Rapid-Scan, etc., and includes both quantitative and qualitative measurements. For further details, see the hybridization methods described above and below. Determining by such hybridization whether the target is differentially expressed (e.g., up-regulated or

differentially-regulated) in the sample can also be accomplished by any effective means. For instance, the target's expression pattern in the sample can be compared to its pattern in a known standard, such as in a normal tissue, or it can be compared to another gene in the same sample. When a second sample is utilized for the comparison, it can be a sample of normal tissue that is known not to contain diseased cells. The comparison can be performed on samples which contain the same amount of RNA (such as polyadenylated RNA or total RNA), or, on RNA extracted from the same amounts of starting tissue. Such a second sample can also be referred to as a control or standard. Hybridization can also be compared to a second target in the same tissue sample. Experiments can be performed that determine a ratio between the target nucleic acid and a second nucleic acid (a standard or control) , e.g., in a normal tissue. When the ratio between the target and control are substantially the same in a normal and sample, the sample is determined or diagnosed not to contain cells. However, if the ratio is different between the normal and sample tissues, the sample is determined to contain cancer cells. The approaches can be combined, and one or more second samples, or second targets can be used. Any second target nucleic acid can be used as a comparison, including "housekeeping" genes, such as beta-actin, alcohol dehydrogenase, or any other gene whose expression does not vary depending upon the disease status of the cell.

Methods of identifying polymorphisms, mutations, etc., of a differentially-regulated gene

Polynucleotides of the present invention can also be utilized to identify mutant alleles, SNPs, gene rearrangements and modifications, and other polymorphisms of the wild-type gene. Mutant alleles, polymorphisms, SNPs, etc., can be identified and isolated from cancers that are known, or suspected to have, a genetic component. Identification of such genes can be carried out routinely (see, above for more guidance), e.g., using PCR, hybridization techniques, direct sequencing, mismatch reactions (see, e.g., above), RFLP analysis, SSCP (e.g., Orita et al., *Proc. Natl. Acad. Sci.*, 86:2766, 1992), etc., where a polynucleotide having a sequence selected from Tables 1 and 2 is used as a probe, or genomic sequences thereof. The selected mutant alleles, SNPs, polymorphisms, etc., can be used diagnostically to determine whether a subject has, or is susceptible to a disorder associated with a differentially-regulated gene, as well as to design therapies and predict the outcome of the disorder. Methods involve, e.g., diagnosing a disorder associated with a differentially-regulated gene or determining susceptibility to a disorder, comprising, detecting the presence of a mutation in a gene selected from Tables 1 and 2. The detecting can be carried out by any

effective method, e.g., obtaining cells from a subject, determining the gene sequence or structure of a target gene (using, e.g., mRNA, cDNA, genomic DNA, etc), comparing the sequence or structure of the target gene to the structure of the normal gene, whereby a difference in sequence or structure indicates a mutation in the gene in the subject. Polynucleotides can also be used to test for mutations, SNPs, polymorphisms, etc., e.g., using mismatch DNA repair technology as described in U.S. Pat. No. 5,683,877; U.S. Pat. No. 5,656,430; Wu et al., *Proc. Natl. Acad. Sci.*, 89:8779-8783, 1992.

The present invention also relates to methods of detecting polymorphisms in a differentially-regulated gene, comprising, e.g., comparing the structure of: genomic DNA comprising all or part of said gene, mRNA comprising all or part of said gene, cDNA comprising all or part of said gene, or a polypeptide comprising all or part of said gene, with the structure of said gene as set forth herein. The methods can be carried out on a sample from any source, e.g., cells, tissues, body fluids, blood, urine, stool, hair, egg, sperm, etc.

These methods can be implemented in many different ways. For example, "comparing the structure" steps include, but are not limited to, comparing restriction maps, nucleotide sequences, amino acid sequences, RFLPs, DNAse sites, DNA methylation fingerprints (e.g., U.S. Pat. No. 6,214,556), protein cleavage sites, molecular weights, electrophoretic mobilities, charges, ion mobility, etc., between a standard gene and a test gene. The term "structure" can refer to any physical characteristics or configurations which can be used to distinguish between nucleic acids and polypeptides. The methods and instruments used to accomplish the comparing step depends upon the physical characteristics which are to be compared. Thus, various techniques are contemplated, including, e.g., sequencing machines (both amino acid and polynucleotide), electrophoresis, mass spectrometer (U.S. Pat. Nos. 6,093,541, 6,002,127), liquid chromatography, HPLC, etc.

To carry out such methods, "all or part" of the gene or polypeptide can be compared. For example, if nucleotide sequencing is utilized, the entire gene can be sequenced, including promoter, introns, and exons, or only parts of it can be sequenced and compared, e.g., exon 1, exon 2, etc.

Mutagenesis

Mutated polynucleotide sequences of the present invention are useful for various

purposes, e.g., to create mutations of the polypeptides they encode, to identify functional regions of genomic DNA, to produce probes for screening libraries, etc. Mutagenesis can be carried out routinely according to any effective method, e.g., oligonucleotide-directed (Smith, M., *Ann. Rev. Genet.*19:423-463, 1985), degenerate oligonucleotide-directed (Hill et al., *Method Enzymology*, 155:558-568, 1987), region-specific (Myers et al., *Science*, 229:242-246, 1985; Derbyshire et al., *Gene*, 46:145, 1986; Ner et al., *DNA*, 7:127, 1988), linker-scanning (McKnight and Kingsbury, *Science*, 217:316-324, 1982), directed using PCR, recursive ensemble mutagenesis (Arkin and Yourvan, *Proc. Natl. Acad. Sci.*, 89:7811-7815, 1992), random mutagenesis (e.g., U.S. Pat. Nos. 5,096,815; 5,198,346; and 5,223,409), site-directed mutagenesis (e.g., Walder et al., *Gene*, 42:133, 1986; Bauer et al., *Gene*, 37:73, 1985; Craik, *Bio Techniques*, January 1985, 12-19; Smith et al., *Genetic Engineering: Principles and Methods*, Plenum Press, 1981), phage display (e.g., Lowman et al., *Biochem.* 30:10832-10837, 1991; Ladner et al., U.S. Pat. No. 5,223,409; Huse, WIPO Publication WO 92/06204), etc. Desired sequences can also be produced by the assembly of target sequences using mutually priming oligonucleotides (Uhlmann, *Gene*, 71:29-40, 1988). For directed mutagenesis methods, analysis of the three-dimensional structure of a polypeptide can be used to guide and facilitate making mutants which effect polypeptide activity. Sites of substrate-enzyme interaction or other biological activities can also be determined by analysis of crystal structure as determined by such techniques as nuclear magnetic resonance, crystallography or photoaffinity labeling. See, for example, de Vos et al., Science 255:306-312, 1992; Smith et al., J. Mol. Biol. 224:899-904, 1992; Wlodaver et al., FEBS Lett. 309:59-64, 1992.

In addition, libraries of differentially-regulated genes and fragments thereof can be used for screening and selection of gene variants. For instance, a library of coding sequences can be generated by treating a double-stranded DNA with a nuclease under conditions where the nicking occurs, e.g., only once per molecule, denaturing the double-stranded DNA, renaturing it to for double-stranded DNA that can include sense/antisense pairs from different nicked products, removing single-stranded portions from reformed duplexes by treatment with S1 nuclease, and ligating the resulting DNAs into an expression vecore. By this method, expression libraries can be made comprising "mutagenized" differentially-regulated genes. The entire coding sequence or parts thereof can be used.

Polynucleotide expression, polypeptides produced thereby, and specific-binding partners thereto.

A polynucleotide according to the present invention can be expressed in a variety of different systems, in vitro and in vivo, according to the desired purpose. For example, a polynucleotide can be inserted into an expression vector, introduced into a desired host, and cultured under conditions effective to achieve expression of a polypeptide coded for by the polynucleotide, to search for specific binding partners. Effective conditions include any culture conditions which are suitable for achieving production of the polypeptide by the host cell, including effective temperatures, pH, medium, additives to the media in which the host cell is cultured (e.g., additives which amplify or induce expression such as butyrate, or methotrexate if the coding polynucleotide is adjacent to a dhfr gene), cycloheximide, cell densities, culture dishes, etc. A polynucleotide can be introduced into the cell by any effective method including, e.g., naked DNA, calcium phosphate precipitation, electroporation, injection, DEAE-Dextran mediated transfection, fusion with liposomes, association with agents which enhance its uptake into cells, viral transfection. A cell into which a polynucleotide of the present invention has been introduced is a transformed host cell. The polynucleotide can be extrachromosomal or integrated into a chromosome(s) of the host cell. It can be stable or transient. An expression vector is selected for its compatibility with the host cell. Host cells include, mammalian cells, e.g., COS, CV1, BHK, CHO, HeLa, LTK, NIH 3T3, PC-3 (CRL-1435), LNCaP (CRL-1740), CA-HPV-10 (CRL-2220), PZ-HPV-7 (CRL-2221), MDA-PCa 2b (CRL-2422), 22Rv1 (CRL2505), NCI-H660 (CRL-5813), HS 804.Sk (CRL-7535), LNCaP-FGF (CRL-10995), RWPE-1 (CRL-11609), RWPE-2 (CRL-11610), PWR-1E (CRL 11611), rat MAT-Ly-LuB-2 (CRL-2376), and other prostate cells, insect cells, such as Sf9 (S. frugipeda) and Drosophila, bacteria, such as E. coli, Streptococcus, bacillus, yeast, such as Sacharomyces, S. cerevisiae, fungal cells, plant cells, embryonic or adult stem cells (e.g., mammalian, such as mouse or human).

Expression control sequences are similarly selected for host compatibility and a desired purpose, e.g., high copy number, high amounts, induction, amplification, controlled expression. Other sequences which can be employed include enhancers such as from SV40, CMV, RSV, inducible promoters, cell-type specific elements, or sequences which allow selective or specific cell expression. Promoters that can be used to drive its expression, include, e.g., the endogenous promoter, MMTV, SV40, trp, lac, tac, or T7 promoters for bacterial hosts; or alpha factor, alcohol oxidase, or PGH promoters for yeast. RNA

promoters can be used to produced RNA transcripts, such as T7 or SP6. See, e.g., Melton et al., *Polynucleotide Res.*, 12(18):7035-7056, 1984; Dunn and Studier. *J. Mol. Bio.*, 166:477-435, 1984; U.S. Pat. No. 5,891,636; Studier et al., *Gene Expression Technology, Methods in Enzymology*, 85:60-89, 1987. In addition, as discussed above, translational signals (including in-frame insertions) can be included.

When a polynucleotide is expressed as a heterologous gene in a transfected cell line, the gene is introduced into a cell as described above, under effective conditions in which the gene is expressed. The term "heterologous" means that the gene has been introduced into the cell line by the "hand-of-man." Introduction of a gene into a cell line is discussed above. The transfected (or transformed) cell expressing the gene can be lysed or the cell line can be used intact.

For expression and other purposes, a polynucleotide can contain codons found in a naturally-occurring gene, transcript, or cDNA, for example, e.g., as set forth in Tables 1 and 2, or it can contain degenerate codons coding for the same amino acid sequences. For instance, it may be desirable to change the codons in the sequence to optimize the sequence for expression in a desired host. See, e.g., U.S. Pat. Nos. 5,567,600 and 5,567,862.

A polypeptide according to the present invention can be recovered from natural sources, transformed host cells (culture medium or cells) according to the usual methods, including, detergent extraction (e.g., non-ionic detergent, Triton X-100, CHAPS, octylglucoside, Igepal CA-630), ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, hydroxyapatite chromatography, lectin chromatography, gel electrophoresis. Protein refolding steps can be used, as necessary, in completing the configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for purification steps. Another approach is express the polypeptide recombinantly with an affinity tag (Flag epitope, HA epitope, myc epitope, 6xHis, maltose binding protein, chitinase, etc) and then purify by anti-tag antibody-conjugated affinity chromatography.

The present invention also relates to antibodies, and other specific-binding partners, which are specific for polypeptides encoded by polynucleotides of the present invention. Antibodies, e.g., polyclonal, monoclonal, recombinant, chimeric, humanized, single-chain, Fab, and fragments thereof, can be prepared according to any desired method. See, also, screening recombinant immunoglobulin libraries (e.g., Orlandi et al., *Proc. Natl. Acad. Sci.*,

86:3833-3837, 1989; Huse et al., *Science*, 256:1275-1281, 1989); in vitro stimulation of lymphocyte populations; Winter and Milstein, *Nature*, 349: 293-299, 1991. The antibodies can be IgM, IgG, subtypes, IgG2a, IgG1, etc. Antibodies, and immune responses, can also be generated by administering naked DNA See, e.g., U.S. Pat. Nos. 5,703,055; 5,589,466; 5,580,859. Antibodies can be used from any source, including, goat, rabbit, mouse, chicken (e.g., IgY; see, Duan, W0/029444 for methods of making antibodies in avian hosts, and harvesting the antibodies from the eggs). An antibody specific for a polypeptide means that the antibody recognizes a defined sequence of amino acids within or including the polypeptide. Other specific binding partners include, e.g., aptamers and PNA, can be prepared against specific epitopes or domains of differentially regulated genes.

The preparation of polyclonal antibodies is well-known to those skilled in the art. See, for example, Green et al., Production of Polyclonal Antisera, in IMMUNOCHEMICAL PROTOCOLS (Manson, ed.), pages 1-5 (Humana Press 1992); Coligan et al., Production of Polyclonal Antisera in Rabbits, Rats, Mice and Hamsters, in CURRENT PROTOCOLS IN IMMUNOLOGY, section 2.4.1 (1992). The preparation of monoclonal antibodies likewise is conventional. See, for example, Kohler & Milstein, Nature 256:495 (1975); Coligan et al., sections 2.5.1-2.6.7; and Harlow et al., ANTIBODIES: A LABORATORY MANUAL, page 726 (Cold Spring Harbor Pub. 1988).

Antibodies can also be humanized, e.g., where they are to be used therapeutically. Humanized monoclonal antibodies are produced by transferring mouse complementarity determining regions from heavy and light variable chains of the mouse immunoglobulin into a human variable domain, and then substituting human residues in the framework regions of the murine counterparts. The use of antibody components derived from humanized monoclonal antibodies obviates potential problems associated with the immunogenicity of murine constant regions. General techniques for cloning murine immunoglobulin variable domains are described, for example, by Orlandi et al., Proc. Nat 'l Acad. Sci. USA 86:3833 (1989), which is hereby incorporated in its entirety by reference. Techniques for producing humanized monoclonal antibodies are described, for example, in U.S. Pat. No. 6,054,297, Jones et al., Nature 321: 522 (1986); Riechmann et al., Nature 332: 323 (1988); Verhoeyen et al., Science 239: 1534 (1988); Carter et al., Proc. Nat'l Acad. Sci. USA 89: 4285 (1992); Sandhu, Crit. Rev. Biotech. 12: 437 (1992); and Singer et al., J. Immunol. 150: 2844 (1993).

Antibodies of the invention also may be derived from human antibody fragments isolated from a combinatorial immunoglobulin library. See, for example, Barbas et al., METHODS: A COMPANION TO METHODS IN ENZYMOLOGY, VOL. 2, page 119 (1991); Winter et al., Ann. Rev. Immunol. 12: 433 (1994). Cloning and expression vectors that are useful for producing a human immunoglobulin phage library can be obtained commercially, for example, from STRATAGENE Cloning Systems (La Jolla, Calif.).

In addition, antibodies of the present invention may be derived from a human monoclonal antibody. Such antibodies are obtained from transgenic mice that have been "engineered" to produce specific human antibodies in response to antigenic challenge. In this technique, elements of the human heavy and light chain loci are introduced into strains of mice derived from embryonic stem cell lines that contain targeted disruptions of the endogenous heavy and light chain loci. The transgenic mice can synthesize human antibodies specific for human antigens and can be used to produce human antibody-secreting hybridomas. Methods for obtaining human antibodies from transgenic mice are described, e.g., in Green et al., Nature Genet. 7:13 (1994); Lonberg et al., Nature 368:856 (1994); and Taylor et al., Int. Immunol. 6:579 (1994).

Antibody fragments of the present invention can be prepared by proteolytic hydrolysis of the antibody or by expression in E. coli of nucleic acid encoding the fragment. Antibody fragments can be obtained by pepsin or papain digestion of whole antibodies by conventional methods. For example, antibody fragments can be produced by enzymatic cleavage of antibodies with pepsin to provide a 5S fragment denoted F(ab').sub.2. This fragment can be further cleaved using a thiol reducing agent, and optionally a blocking group for the sulfhydryl groups resulting from cleavage of disulfide linkages, to produce 3.5S Fab' monovalent fragments. Alternatively, an enzymatic cleavage using pepsin produces two monovalent Fab' fragments and an Fc fragment directly. These methods are described, for example, by Goldenberg, U.S. Pat. No. 4,036,945 and No. 4,331,647, and references contained therein. These patents are hereby incorporated in their entireties by reference. See also Nisoiihoff et al., Arch. Biochem. Biophys. 89:230 (1960); Porter, Biochem. J. 73:119 (1959); Edelman etal, METHODS IN ENZYMOLOGY, VOL. 1, page 422 (Academic Press 1967); and Coligan et al. at sections 2.8.1-2.8.10 and 2.10.1-2.10.4.

Other methods of cleaving antibodies, such as separation of heavy chains to form monovalent light-heavy chain fragments, further cleavage of fragments, or other enzymatic, chemical, or genetic techniques can also be used. For example, Fv fragments comprise an association of V.sub.H and V.sub.L chains. This association may be noncovalent, as described in Inbar et al., Proc. Nat'l Acad. Sci. USA 69:2659 (1972). Alternatively, the

variable chains can be linked by an intermolecular disulfide bond or cross-linked by chemicals such as glutaraldehyde. See, e.g., Sandhu, supra. Preferably, the Fv fragments comprise V.sub.H and V.sub.L chains connected by a peptide linker. These single-chain antigen binding proteins (sFv) are prepared by constructing a structural gene comprising nucleic acid sequences encoding the V.sub.H and V.sub.L domains connected by an oligonucleotide. The structural gene is inserted into an expression vector, which is subsequently introduced into a host cell such as E. coli. The recombinant host cells synthesize a single polypeptide chain with a linker peptide bridging the two V domains. Methods for producing sFvs are described, for example, by Whitlow et al., METHODS: A COMPANION TO METHODS IN ENZYMOLOGY, VOL. 2, page 97 (1991); Bird etal.,Science 242:423-426 (1988); Ladneret al., U.S. Pat. No. 4,946,778; Pack et al., Bio/Technology 11: 1271-77 (1993); and Sandhu, supra.

Another form of an antibody fragment is a peptide coding for a single complementarity-determining region (CDR). CDR peptides ("minimal recognition units") can be obtained by constructing genes encoding the CDR of an antibody of interest. Such genes are prepared, for example, by using the polymerase chain reaction to synthesize the variable region from RNA of antibody-producing cells. See, for example, Larrick et al., METHODS: A COMPANION TO METHODS IN ENZYMOLOGY, VOL. 2, page 106 (1991).

The term "antibody" as used herein includes intact molecules as well as fragments thereof, such as Fab, F(ab')2, and Fv which are capable of binding to an epitopic determinant present in Bin1 polypeptide. Such antibody fragments retain some ability to selectively bind with its antigen or receptor. The term "epitope" refers to an antigenic determinant on an antigen to which the paratope of an antibody binds. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. Antibodies can be prepared against specific epitopes or polypeptide domains.

Antibodies which bind to a differentially-regulated polypeptide of the present invention can be prepared using an intact polypeptide or fragments containing small peptides of interest as the immunizing antigen. For example, it may be desirable to produce antibodies that specifically bind to the N- or C-terminal domains of said polypeptide. The polypeptide or peptide used to immunize an animal which is derived from translated cDNA or chemically synthesized which can be conjugated to a carrier protein, if desired. Such commonly used

carriers which are chemically coupled to the immunizing peptide include keyhole limpet hemocyanin (KLH), thyroglobulin, bovine serum albumin (BSA), and tetanus toxoid.

Polyclonal or monoclonal antibodies can be further purified, for example, by binding to and elution from a matrix to which the polypeptide or a peptide to which the antibodies were raised is bound. Those of skill in the art will know of various techniques common in the immunology arts for purification and/or concentration of polyclonal antibodies, as well as monoclonal antibodies (See for example, Coligan, et al., Unit 9, *Current Protocols in Immunology*, Wiley Interscience, 1994, incorporated by reference).

Anti-idiotype technology can also be used to produce invention monoclonal antibodies which mimic an epitope. For example, an anti-idiotypic monoclonal antibody made to a first monoclonal antibody will have a binding domain in the hypervariable region which is the "image" of the epitope bound by the first monoclonal antibody.

Methods of detecting polypeptides

Polypeptides coded for by a differentially-regulated gene of the present invention can be detected, visualized, determined, quantitated, etc. according to any effective method. useful methods include, e.g., but are not limited to, immunoassays, RIA (radioimmunassay), ELISA, (enzyme-linked-immunosorbent assay), immunoflourescence, flow cytometry, histology, electron microscopy, light microscopy, in situ assays, immunoprecipitation, Western blot, etc.

Immunoassays may be carried in liquid or on biological support. For instance, a sample (e.g., blood, stool, urine, cells, tissue, body fluids, etc.) can be brought in contact with and immobilized onto a solid phase support or carrier such as nitrocellulose, or other solid support that is capable of immobilizing cells, cell particles or soluble proteins. The support may then be washed with suitable buffers followed by treatment with the detectably labeled differentially-regulated gene specific antibody. The solid phase support can then be washed with a buffer a second time to remove unbound antibody. The amount of bound label on solid support may then be detected by conventional means.

A "solid phase support or carrier" includes any support capable of binding an antigen, antibody, or other specific binding partner. Supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, and magnetite. A support material can have any structural or physical configuration. Thus, the support configuration may be spherical, as in a bead, or cylindrical,

as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the surface may be flat such as a sheet, test strip, etc. Preferred supports include polystyrene beads

One of the many ways in which gene peptide-specific antibody can be detectably labeled is by linking it to an enzyme and using it in an enzyme immunoassay (EIA). See, e.g., Voller, A., "The Enzyme Linked Immunosorbent Assay (ELISA)," 1978, Diagnostic Horizons 2, 1-7, Microbiological Associates Quarterly Publication, Walkersville, Md.); Voller, A. et al., 1978, J. Clin. Pathol. 31, 507-520; Butler, J. E., 1981, Meth. Enzymol. 73, 482-523; Maggio, E. (ed.), 1980, Enzyme Immunoassay, CRC Press, Boca Raton, Fla.. The enzyme which is bound to the antibody will react with an appropriate substrate, preferably a chromogenic substrate, in such a manner as to produce a chemical moiety that can be detected, for example, by spectrophotometric, fluorimetric or by visual means. Enzymes that can be used to detectably label the antibody include, but are not limited to, malate dehydrogenase, staphylococcal nuclease, delta-5-steroid isomerase, yeast alcohol dehydrogenase, .alpha.-glycerophosphate, dehydrogenase, triose phosphate isomerase, horseradish peroxidase, alkaline phosphatase, asparaginase, glucose oxidase, .beta.-galactosidase, ribonuclease, urease, catalase, glucose-6-phosphate dehydrogenase, glucoamylase and acetylcholinesterase. The detection can be accomplished by colorimetric methods that employ a chromogenic substrate for the enzyme. Detection may also be accomplished by visual comparison of the extent of enzymatic reaction of a substrate in comparison with similarly prepared standards.

Detection may also be accomplished using any of a variety of other immunoassays. For example, by radioactively labeling the antibodies or antibody fragments, it is possible to detect differentially-regulated peptides through the use of a radioimmunoassay (RIA). See, e.g., Weintraub, B., Principles of Radioimmunoassays, Seventh Training Course on Radioligand Assay Techniques, The Endocrine Society, March, 1986. The radioactive isotope can be detected by such means as the use of a gamma counter or a scintillation counter or by autoradiography.

It is also possible to label the antibody with a fluorescent compound. When the fluorescently labeled antibody is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycoerythrin, phycocyanin, allophycocyanin, o-phthaldehyde and fluorescamine. The antibody can also be detectably

labeled using fluorescence emitting metals such as those in the lanthanide series. These metals can be attached to the antibody using such metal chelating groups as diethylenetriaminepentacetic acid (DTPA) or ethylenediaminetetraacetic acid (EDTA).

The antibody also can be detectably labeled by coupling it to a chemiluminescent compound. The presence of the chemiluminescent-tagged antibody is then determined by detecting the presence of luminescence that arises during the course of a chemical reaction. Examples of useful chemiluminescent labeling compounds are luminol, isoluminol, theromatic acridinium ester, imidazole, acridinium salt and oxalate ester.

Likewise, a bioluminescent compound may be used to label the antibody of the present invention. Bioluminescence is a type of chemiluminescence found in biological systems in which a catalytic protein increases the efficiency of the chemiluminescent reaction. The presence of a bioluminescent protein is determined by detecting the presence of luminescence. Important bioluminescent compounds for purposes of labeling are luciferin, luciferase and aequorin.

Tissue and Disease

The prostate is a secretory organ surrounding the neck of the bladder and urethra. Its primary function is to produce fluids and other materials necessary for sperm transport and maintenance. Structurally, it has both glandular and nonglandular components. The glandular component is predominantly comprised of ducts and acini responsible for the production and transport prostatic fluids. Epithelial cells are the main identifiable cell found in these regions, primarily of the basal and secretory types, but also endocrine-paracrine and transitional epithelial. The non-glandular component contains the capsular and muscle tissues, which, respectively, hold the organ together and function in fluid discharge. See, e.g., Histology for Pathologists, Sternberg, S.S., editor, Raven Press, NY, 1992, Chapter 40.

The major diseases of the prostate include, e.g., prostatic hyperplasia (BPH), prostatitis, and prostate cancer (e.g., prostatic adenocarcinoma). BPH is a benign, proliferative disease of the prostatic epithelial cells. While it may cause urinary tract obstruction in some patients, for the most part, it is generally asymptomatic. Prostate cancer, on the other hand, is the most common form of cancer in white males in the United States, occurring predominantly in males over age 50. The prevalence of prostate diseases, such as prostate cancer, has made the discovery of prostate selective markers and gene expression patterns of great importance.

The most common scale of assessing prostate pathology is the Gleason grading system. See, e.g., Bostwick, *Am. J. Clin. Path.*, 102: s38-s56, 1994. Once the cancer is identified, staging can assess the size, location, and extent of the cancer. Several different staging scales are commonly used, including stages A-D, and Tumor-Nodes-Metastases (TNM). For treatment, diagnosis, staging, etc., of prostate conditions, methods can be carried out analogously to, and in combination with, U.S. Pat. Nos. 6,107,090; 6,057,116; 6,034,218; 6,004,267; 5,919,638; 5,882,864; 5,763,202; 5,747,264; 5,688,649; 5,552,277.

In addition, the present invention relates to methods of assessing a therapeutic or preventative intervention in a subject having a prostate cancer, comprising, e.g., detecting the expression levels of differentially-regulated target genes, wherein the target genes comprise a gene which is represented by a sequence selected from Tables 1 and 2, or, a gene represented by a sequence having 95% sequence identity or more to a sequence selected from Tables 1 and 2. By "therapeutic or preventative intervention," it is meant, e.g., a drug administered a patient, surgery, radiation, chemotherapy, and other measures taken to prevent a cancer or treat a cancer.

Grading, staging, comparing, assessing, methods and compositions

The present invention also relates to methods and compositions for staging and grading cancers. As already defined, staging relates to determining the extent of a cancer's spread, including its size and the degree to which other tissues, such as lymph nodes are involved in the cancer. Grading refers to the degree of a cell's retention of the characteristics of the tissue of its origin. A lower grade cancer comprises tumor cells that more closely resemble normal cells than a medium or higher grade cancer. Grading can be a useful diagnostic and prognostic tool. Higher grade cancers usually behave more aggressively than lower grade cancers. Thus, knowledge of the cancer grade, as well as its stage, can be a significant factor in the choice of the appropriate therapeutic intervention for the particular patient, e.g., surgery, radiation, chemotherapy, etc. Staging and grading can also be used in conjunction with a therapy to assess its efficacy, to determine prognosis, to determine effective dosages, etc.

Various methods of staging and grading cancers can be employed in accordance with the present invention. A "cell expression profile" or "cell expression fingerprint" is a representation of the expression of various different genes (e.g., polynucleotide sequences of SEQ ID NOS 1-107) in a given cell or sample comprising cells. These cell expression

profiles can be useful as reference standards. The cell expression fingerprints can be used alone for grading, or in combination with other grading methods.

The present invention also relates to methods and compositions for diagnosing a prostate cancer, or determining susceptibility to a prostate cancer, using polynucleotides, polypeptides, and specific-binding partners of the present invention to detect, assess, determine, etc., differentially-regulated genes of the present invention. In such methods, the gene can serve as a marker for prostate cancer, e.g., where the gene, when mutant, is a direct cause of the prostate cancer; where the gene is affected by another gene(s) which is directly responsible for the prostate cancer, e.g., when the gene is part of the same signaling pathway as the directly responsible gene; and, where the gene is chromosomally linked to the gene(s) directly responsible for the prostate cancer, and segregates with it. Many other situations are possible. To detect, assess, determine, etc., a probe specific for the gene can be employed as described above and below. Any method of detecting and/or assessing the gene can be used, including detecting expression of the gene using polynucleotides, antibodies, or other specific-binding partners.

The present invention relates to methods of diagnosing a disorder associated with prostate cancer, or determining a subject's susceptibility to such prostate cancer, comprising, e.g., assessing the expression of a differentially-regulated gene in a tissue sample comprising tissue or cells suspected of having prostate cancer (e.g., where the sample comprises prostate). The phrase "diagnosing" indicates that it is determined whether the sample has a prostate cancer cells. "Determining a subject's susceptibility to a prostate cancer" indicates that the subject is assessed for whether s/he is predisposed to get such a disease or disorder, where the predisposition is indicated by abnormal expression of the gene (e.g., gene mutation, gene expression pattern is not normal, etc.). Predisposition or susceptibility to a disease may result when a such disease is influenced by epigenetic, environmental, etc., factors.

By the phrase "assessing expression of a differentially-regulated gene," it is meant that the functional status of the gene is evaluated. This includes, but is not limited to, measuring expression levels of said gene, determining the genomic structure of said gene, determining the mRNA structure of transcripts from said gene, or measuring the expression levels of polypeptide coded for by said gene. Thus, the term "assessing expression" includes evaluating the all aspects of the transcriptional and translational machinery of the gene. For instance, if a promoter defect causes, or is suspected of

causing, the disorder, then a sample can be evaluated (i.e., "assessed") by looking (e.g., sequencing or restriction mapping) at the promoter sequence in the gene, by detecting transcription products (e.g., RNA), by detecting translation product (e.g., polypeptide). Any measure of whether the gene is functional can be used, including, polypeptide, polynucleotide, and functional assays for the gene's biological activity.

In making the assessment, it can be useful to compare the results to a normal gene, e.g., a gene which is not associated with the disorder. The nature of the comparison can be determined routinely, depending upon how the assessing is accomplished. If, for example, the mRNA levels of a sample is detected, then the mRNA levels of a normal can serve as a comparison, or a gene which is known not to be affected by the disorder. Methods of detecting mRNA are well known, and discussed above, e.g., but not limited to, Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, etc. Similarly, if polypeptide production is used to evaluate the gene, then the polypeptide in a normal tissue sample can be used as a comparison, or, polypeptide from a different gene whose expression is known not to be affected by the disorder. These are only examples of how such a method could be carried out.

Assessing the effects of therapeutic and preventative interventions (e.g., administration of a drug, chemotherapy, radiation, etc.) on prostate cancer is a major effort in drug discovery, clinical medicine, and pharmacogenomics. The evaluation of therapeutic and preventative measures, whether experimental or already in clinical use, has broad applicability, e.g., in clinical trials, for monitoring the status of a patient, for analyzing and assessing animal models, and in any scenario involving cancer treatment and prevention. Analyzing the expression profiles of polynucleotides of the present invention can be utilized as a parameter by which interventions are judged and measured. Treatment of a disorder can change the expression profile in some manner which is prognostic or indicative of the drug's effect on it. Changes in the profile can indicate, e.g., drug toxicity, return to a normal level, etc. Accordingly, the present invention also relates to methods of monitoring or assessing a therapeutic or preventative measure (e.g., chemotherapy, radiation, anti-neoplastic drugs, antibodies, etc.) in a subject having prostate cancer, or, susceptible to such a disorder, comprising, e.g., detecting the expression levels of one or more differentially-regulated genes of the present invention. A subject can be a cell-based assay system, non-human animal model, human patient, etc. Detecting can be accomplished as described for the methods above and below. By

"therapeutic or preventative intervention," it is meant, e.g., a drug administered to a patient, surgery, radiation, chemotherapy, and other measures taken to prevent, treat, or diagnose prostate cancer.

Expression can be assessed in any sample comprising any tissue or cell type, body fluid, etc., as discussed for other methods of the present invention, including cells from prostate can be used, or cells derived from prostate. By the phrase "cells derived from prostate," it is meant that the derived cells originate from prostate, e.g., when metastasis from a primary tumor site has occurred, when a progenitor-type or pluripotent cell gives rise to other cells, etc.

Identifying agent methods

The present invention also relates to methods of identifying agents, and the agents themselves, which modulate prostate cancer genes. These agents can be used to modulate the biological activity of the polypeptide encoded for the gene, or the gene, itself. Agents which regulate the gene or its product are useful in variety of different environments, including as medicinal agents to treat or prevent disorders associated with prostate cancer genes and as research reagents to modify the function of tissues and cell.

Methods of identifying agents generally comprise steps in which an agent is placed in contact with the gene, transcription product, translation product, or other target, and then a determination is performed to assess whether the agent "modulates" the target. The specific method utilized will depend upon a number of factors, including, e.g., the target (i.e., is it the gene or polypeptide encoded by it), the environment (e.g., in vitro or in vivo), the composition of the agent, etc.

For modulating the expression of a prostate cancer gene, a method can comprise, in any effective order, one or more of the following steps, e.g., contacting a prostate cancer gene (e.g., in a cell population) with a test agent under conditions effective for said test agent to modulate the expression of the prostate cancer, and determining whether said test agent modulates said gene. An agent can modulate expression of a gene at any level, including transcription, translation, and/or perdurance of the nucleic acid (e.g., degradation, stability, etc.) in the cell. For modulating the biological activity of prostate cancer polypeptides, a method can comprise, in any effective order, one or more of the following steps, e.g., contacting a polypeptide (e.g., in a cell, lysate, or isolated) with a test agent under conditions

effective for said test agent to modulate the biological activity of said polypeptide, and determining whether said test agent modulates said biological activity.

Contacting a gene or polypeptidewith the test agent can be accomplished by any suitable method and/or means that places the agent in a position to functionally control its expression or biological activity. Functional control indicates that the agent can exert its physiological effect on the gene or polypeptide through whatever mechanism it works. The choice of the method and/or means can depend upon the nature of the agent and the condition and type of environment in which the gene or polypeptide is presented, e.g., lysate, isolated, or in a cell population (such as, *in vivo*, *in vitro*, organ explants, etc.). For instance, if the cell population is an *in vitro* cell culture, the agent can be contacted with the cells by adding it directly into the culture medium. If the agent cannot dissolve readily in an aqueous medium, it can be incorporated into liposomes, or another lipophilic carrier, and then administered to the cell culture. Contact can also be facilitated by incorporation of agent with carriers and delivery molecules and complexes, by injection, by infusion, etc.

After the agent has been administered in such a way that it can gain access to the gene or polypeptide, it can be determined whether the test agent modulates the gene or polypeptide expression or biological activity. Modulation can be of any type, quality, or quantity, e.g., increase, facilitate, enhance, up-regulate, stimulate, activate, amplify, augment, induce, decrease, down-regulate, diminish, lessen, reduce, etc. The modulatory quantity can also encompass any value, e.g., 1%, 5%, 10%, 50%, 75%, 1-fold, 2-fold, 5-fold, 10-fold, 100-fold, etc. To modulate gene expression means, e.g., that the test agent has an effect on its expression, e.g., to effect the amount of transcription, to effect RNA splicing, to effect translation of the RNA into polypeptide, to effect RNA or polypeptide stability, to effect polyadenylation or other processing of the RNA, to effect post-transcriptional or post-translational processing, etc. To modulate biological activity means, e.g., that a functional activity of the polypeptide is changed in comparison to its normal activity in the absence of the agent. This effect includes, increase, decrease, block, inhibit, enhance, etc.

A test agent can be of any molecular composition, e.g., chemical compounds, biomolecules, such as polypeptides, lipids, nucleic acids (e.g., antisense to a polynucleotide sequence selected from Tables 1 and 2, or genomic sequences thereof), carbohydrates, antibodies, ribozymes, double-stranded RNA, aptamers, etc. For example, if a polypeptide to be modulated is a cell-surface molecule, a test agent can be an antibody that specifically recognizes it and, e.g., causes the polypeptide to be internalized, leading to its down

regulation on the surface of the cell. Such an effect does not have to be permanent, but can require the presence of the antibody to continue the down-regulatory effect. Antibodies can also be used to modulate the biological activity a polypeptide in a lysate or other cell-free form. Antisense can also be used as test agents to modulate gene expression.

Markers

The polynucleotides of the present invention can be used with other markers, especially prostate and prostate cancer markers to identity, detect, stage, diagnosis, determine, prognosticate, treat, etc., tissue, diseases and conditions, etc, of the prostate. Markers can be polynucleotides, polypeptides, antibodies, ligands, specific binding partners, etc.

A number of genes and gene products have been identified which are associated with prostate cancer metastasis and/or progression, e.g., PSA, KAI1 (shows decreased expression in metastatic cells; Dong et al., *Science*, 268:884-6, 1995), D44 isoforms (differentially-regulated during carcinoma progression; Noordzij et al., *Clin. Cancer Res.*, 3:805-15, 1997), p53 (Effert et al., *J. Urol.*, 150:257-61, 1993), Rb, CDKN2, E-cadherin, PTEN (Hamilton et al., *Br. J. Cancer*, 82:1671-6, 2000; Dong et al., *Clin. Cancer Res.*, 7:304-308, 2001), bcl-2, prostatic acid phosphatase (PAP), prostate specific membrane antigen (e.g., U.S. Pat. Nos. 5,538,866 and 6,107,090), Smad3 (e.g., Kang et al., *Proc. Natl. Acad. Sci.*, 98:3018-3023, 2001), TGF-beta, and other oncogenes and tumor suppressor genes. See, also, Myers and Grizzle, *Eur. Urol.*, 30:153-166, 1996, for other biomarkers associated with prostatic carcinoma, such as PCNA, p185-erbB-2, p180erbB-3, TAG-72, nm23-H1 and FASE. Such markers can be used in combination with the methods of the present invention to facilitate identifying, grading, staging, prognostication, etc, of conditions and diseases of the prostate.

Therapeutics

Selective polynucleotides, polypeptides, and specific-binding partners thereto, can be utilized in therapeutic applications, especially to treat prostate cancer. Useful methods include, but are not limited to, immunotherapy (e.g., using specific-binding partners to polypeptides), vaccination (e.g., using a selective polypeptide or a naked DNA encoding such polypeptide), protein or polypeptide replacement therapy, gene therapy (e.g., germ-line correction, antisense), etc.

Various immunotherapeutic approaches can be used. For instance, unlabeled

antibody that specifically recognizes a tissue-specific antigen can be used to stimulate the body to destroy or attack the cancer, to cause down-regulation, to produce complement-mediated lysis, to inhibit cell growth, etc., of target cells which display the antigen, e.g., analogously to how c-erbB-2 antibodies are used to treat breast cancer. In addition, antibody can be labeled or conjugated to enhance its deleterious effect, e.g., with radionuclides and other energy emitting entitities, toxins, such as ricin, exotoxin A (ETA), and diphtheria, cytotoxic or cytostatic agents, immunomodulators, chemotherapeutic agents, etc. See, e.g., U.S. Pat. No. 6,107,090.

An antibody or other specific-binding partner can be conjugated to a second molecule, such as a cytotoxic agent, and used for targeting the second molecule to a tissue-antigen positive cell (Vitetta, E. S. et al., 1993, Immunotoxin therapy, in DeVita, Jr., V. T. et al., eds, Cancer: Principles and Practice of Oncology, 4th ed., J. B. Lippincott Co., Philadelphia, 2624-2636). Examples of cytotoxic agents include, but are not limited to, antimetabolites, alkylating agents, anthracyclines, antibiotics, anti-mitotic agents, radioisotopes and chemotherapeutic agents. Further examples of cytotoxic agents include, but are not limited to ricin, doxorubicin, daunorubicin, taxol, ethidium bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, 1-dehydrotestosterone, diptheria toxin, Pseudomonas exotoxin (PE) A, PE40, abrin, elongation factor-2 and glucocorticoid. Techniques for conjugating therapeutic agents to antibodies are well.

In addition to immunotherapy, polynucleotides and polypeptides can be used as targets for non-immunotherapeutic applications, e.g., using compounds which interfere with function, expression (e.g., antisense as a therapeutic agent), assembly, etc. RNA interference can be used in vivtro and in vivo to silence differentially-expressed genes when its expression contributes to a disease (but also for other purposes, e.g., to identify the gene's function to change a developmental pathway of a cell, etc.). See, e.g., Sharp and Zamore, *Science*, 287:2431-2433, 2001; Grishok et al., *Science*, 287:2494, 2001.

Delivery of therapeutic agents can be achieved according to any effective method, including, liposomes, viruses, plasmid vectors, bacterial delivery systems, orally, systemically, etc. Therapeutic agents of the present invention can be administered in any form by any effective route, including, e.g., oral, parenteral, enteral, intraperitoneal, topical, transdermal (e.g., using any standard patch), ophthalmic, nasally, local, non-oral, such as aerosal, inhalation, subcutaneous, intramuscular, buccal, sublingual, rectal, vaginal, intra-

arterial, and intrathecal, etc. They can be administered alone, or in combination with any ingredient(s), active or inactive.

In addition to therapeutics, *per se*, the present invention also relates to methods of treating prostate cancer showing altered expression of differentially-regulated genes, such as Tables 1 and 2, comprising, e.g., administering to a subject in need thereof a therapeutic agent which is effective for regulating expression of said genes and/or which is effective in treating said disease. The term "treating" is used conventionally, e.g., the management or care of a subject for the purpose of combating, alleviating, reducing, relieving, improving the condition of, etc., of a disease or disorder. By the phrase "altered expression," it is meant that the disease is associated with a mutation in the gene, or any modification to the gene (or corresponding product) which affects its normal function. Thus, expression of a differentially-regulated gene refers to, e.g., transcription, translation, splicing, stability of the mRNA or protein product, activity of the gene product, differential expression, etc.

Any agent which "treats" the disease can be used. Such an agent can be one which regulates the expression of the gene. Expression refers to the same acts already mentioned, e.g. transcription, translation, splicing, stability of the mRNA or protein product, activity of the gene product, differential expression, etc. For instance, if the condition was a result of a complete deficiency of the gene product, administration of gene product to a patient would be said to treat the disease and regulate the gene's expression. Many other possible situations are possible, e.g., where the gene is aberrantly expressed, and the therapeutic agent regulates the aberrant expression by restoring its normal expression pattern.

Antisense

Antisense polynucleotide (e.g., RNA) can also be prepared from a polynucleotide according to the present invention, preferably an anti-sense to a gene of Tables 1 and 2. Antisense polynucleotide can be used in various ways, such as to regulate or modulate expression of the polypeptides they encode, e.g., inhibit their expression, for in situ hybridization, for therapeutic purposes, for making targeted mutations (in vivo, triplex, etc.) etc. For guidance on administering and designing anti-sense, see, e.g., U.S. Pat. Nos. 6,200,960, 6,200,807, 6,197,584, 6,190,869, 6,190,661, 6,187,587, 6,168,950, 6,153,595, 6,150,162, 6,133,246, 6,117,847, 6,096,722, 6,087,343, 6,040,296, 6,005,095, 5,998,383,

5,994,230, 5,891,725, 5,885,970, and 5,840,708. An antisense polynucleotides can be operably linked to an expression control sequence. A total length of about 35 bp can be used in cell culture with cationic liposomes to facilitate cellular uptake, but for *in vivo* use, preferably shorter oligonucleotides are administered, e.g. 25 nucleotides.

Antisense polynucleotides can comprise modified, nonnaturally-occurring nucleotides and linkages between the nucleotides (e.g., modification of the phosphate-sugar backbone; methyl phosphonate, phosphorothioate, or phosphorodithioate linkages; and 2'-O-methyl ribose sugar units), e.g., to enhance in vivo or in vitro stability, to confer nuclease resistance, to modulate uptake, to modulate cellular distribution and compartmentalization, etc. Any effective nucleotide or modification can be used, including those already mentioned, as known in the art, etc., e.g., disclosed in U.S. Pat. Nos. 6,133,438; 6,127,533; 6,124,445; 6,121,437; 5,218,103 (e.g., nucleoside thiophosphoramidites); 4,973,679; Sproat et al., "2'-O-Methyloligoribonucleotides: synthesis and applications," Oligonucleotides and Analogs A Practical Approach, Eckstein (ed.), IRL Press, Oxford, 1991, 49-86; Iribarren et al., "2'O-Alkyl Oligoribonucleotides as Antisense Probes," Proc. Natl. Acad. Sci. USA, 1990, 87, 7747-7751; Cotton et al., "2'-O-methyl, 2'-O-ethyl oligoribonucleotides and phosphorothioate oligodeoxyribonucleotides as inhibitors of the in vitro U7 snRNP-dependent mRNA processing event," Nucl. Acids Res., 1991, 19, 2629-2635.

Arrays

The present invention also relates to an ordered array of polynucleotide probes and specific-binding partners (e.g., antibodies) for detecting the expression of differentially-regulated genes in a sample, comprising, one or more polynucleotide probes or specific binding partners associated with a solid support, wherein each probe is specific for said genes, and the probes comprise a nucleotide sequence of Tables 1 and 2 which is specific for said gene, a nucleotide sequence having sequence identity to Tables 1 and 2 which is specific for said gene or polynucleotide, or complements thereto, or a specific-binding partner which is specific for said genes.

The phrase "ordered array" indicates that the probes are arranged in an identifiable or position-addressable pattern, e.g., such as the arrays disclosed in U.S. Pat. Nos. 6,156,501, 6,077,673, 6,054 ,270, 5,723,320, 5,700,637, WO09919711, WO00023803. The probes are associated with the solid support in any effective way. For instance, the probes can be bound to the solid support, either by polymerizing the probes on the substrate, or by attaching a

probe to the substrate. Association can be, covalent, electrostatic, noncovalent, hydrophobic, hydrophilic, noncovalent, coordination, adsorbed, absorbed, polar, etc. When fibers or hollow filaments are utilized for the array, the probes can fill the hollow orifice, be absorbed into the solid filament, be attached to the surface of the orifice, etc. Probes can be of any effective size, sequence identity, composition, etc., as already discussed.

Ordered arrays can further comprise polynucleotide probes or specific-binding partners which are specific for other genes, including genes specific for prostate or disorders associated with prostate, such as prostate cancer.

Transgenic animals

The present invention also relates to transgenic animals comprising differentially-regulated genes of the present invention. Such genes, as discussed in more detail below, include, but are not limited to, functionally-disrupted genes, mutated genes, ectopically or selectively-expressed genes, inducible or regulatable genes, etc. These transgenic animals can be produced according to any suitable technique or method, including homologous recombination, mutagenesis (e.g., ENU, Rathkolb et al., *Exp. Physiol.*, 85(6):635-644, 2000), and the tetracycline-regulated gene expression system (e.g., U.S. Pat. No. 6,242,667). The term "gene" as used herein includes any part of a gene, i.e., regulatory sequences, promoters, enhancers, exons, introns, coding sequences, etc. The nucleic acid present in the construct or transgene can be naturally-occurring wild-type, polymorphic, or mutated.

Along these lines, polynucleotides of the present invention can be used to create transgenic animals, e.g. a non-human animal, comprising at least one cell whose genome comprises a functional disruption of a differentially-regulated gene. By the phrases "functional disruption" or "functionally disrupted," it is meant that the gene does not express a biologically-active product. It can be substantially deficient in at least one functional activity coded for by the gene. Expression of a polypeptide can be substantially absent, i.e., essentially undetectable amounts are made. However, polypeptide can also be made, but which is deficient in activity, e.g., where only an amino-terminal portion of the gene product is produced.

The transgenic animal can comprise one or more cells. When substantially all its cells contain the engineered gene, it can be referred to as a transgenic animal "whose genome comprises" the engineered gene. This indicates that the endogenous gene loci of the animal has been modified and substantially all cells contain such modification.

Functional disruption of the gene can be accomplished in any effective way, including, e.g., introduction of a stop codon into any part of the coding sequence such that the resulting polypeptide is biologically inactive (e.g., because it lacks a catalytic domain, a ligand binding domain, etc.), introduction of a mutation into a promoter or other regulatory sequence that is effective to turn it off, or reduce transcription of the gene, insertion of an exogenous sequence into the gene which inactivates it (e.g., which disrupts the production of a biologically-active polypeptide or which disrupts the promoter or other transcriptional machinery), deletion of sequences from the a differentially-regulated gene, etc. Examples of transgenic animals having functionally disrupted genes are well known, e.g., as described in U.S. Pat. Nos. 6,239,326, 6,225,525, 6,207,878, 6,194,633, 6,187,992, 6,180,849, 6,177,610, 6,100,445, 6,087,555, 6,080,910, 6,069,297, 6,060,642, 6,028,244, 6,013,858, 5,981,830, 5,866,760, 5,859,314, 5,850,004, 5,817,912, 5,789,654, 5,777,195, and 5,569,824. A transgenic animal which comprises the functional disruption can also be referred to as a "knock-out" animal, since the biological activity of its a differentially-regulated gene has been "knocked-out." Knock-outs can be homozygous or heterozygous.

For creating functional disrupted genes, and other gene mutations, homologous recombination technology is of special interest since it allows specific regions of the genome to be targeted. Using homologous recombination methods, genes can be specifically-inactivated, specific mutations can be introduced, and exogenous sequences can be introduced at specific sites. These methods are well known in the art, e.g., as described in the patents above. See, also, Robertson, *Biol. Reproduc.*, 44(2):238-245, 1991. Generally, the genetic engineering is performed in an embryonic stem (ES) cell, or other pluripotent cell line (e.g., adult stem cells, EG cells), and that genetically-modified cell (or nucleus) is used to create a whole organism. Nuclear transfer can be used in combination with homologous recombination technologies.

For example, a differentially-regulated gene locus can be disrupted in mouse ES cells using a positive-negative selection method (e.g., Mansour et al., *Nature*, 336:348-352, 1988). In this method, a targeting vector can be constructed which comprises a part of the gene to be targeted. A selectable marker, such as neomycin resistance genes, can be inserted into a a differentially-regulated gene exon present in the targeting vector, disrupting it. When the vector recombines with the ES cell genome, it disrupts the function of the gene. The presence in the cell of the vector can be determined by expression of neomycin resistance. See, e.g., U.S. Pat. No. 6,239,326. Cells having at least one functionally disrupted gene can

be used to make chimeric and germline animals, e.g., animals having somatic and/or germ cells comprising the engineered gene. Homozygous knock-out animals can be obtained from breeding heterozygous knock-out animals. See, e.g., U.S. Pat. No. 6,225,525.

A transgenic animal, or animal cell, lacking one or more functional differentially-regulated genes can be useful in a variety of applications, including, as an animal model for cancer, for drug screening assays, as a source of tissues deficient in said gene activity, and any of the utilities mentioned in any issued U.S. Patent on transgenic animals, including, U.S. Pat. Nos. 6,239,326, 6,225,525, 6,207,878, 6,194,633, 6,187,992, 6,180,849, 6,177,610, 6,100,445, 6,087,555, 6,080,910, 6,069,297, 6,060,642, 6,028,244, 6,013,858, 5,981,830, 5,866,760, 5,859,314, 5,850,004, 5,817,912, 5,789,654, 5,777,195, and 5,569,824.

The present invention also relates to non-human, transgenic animal whose genome comprises recombinant a differentially-regulated gene nucleic acid operatively linked to an expression control sequence effective to express said coding sequence, e.g., in prostate. such a transgenic animal can also be referred to as a "knock-in" animal since an exogenous gene has been introduced, stably, into its genome.

A recombinant a differentially-regulated gene nucleic acid refers to a gene which has been introduced into a target host cell and optionally modified, such as cells derived from animals, plants, bacteria, yeast, etc. A recombinant a differentially-regulated gene includes completely synthetic nucleic acid sequences, semi-synthetic nucleic acid sequences, sequences derived from natural sources, and chimeras thereof. "Operable linkage" has the meaning used through the specification, i.e., placed in a functional relationship with another nucleic acid. When a gene is operably linked to an expression control sequence, as explained above, it indicates that the gene (e.g., coding sequence) is joined to the expression control sequence (e.g., promoter) in such a way that facilitates transcription and translation of the coding sequence. As described above, the phrase "genome" indicates that the genome of the cell has been modified. In this case, the recombinant a differentially-regulated gene has been stably integrated into the genome of the animal. The a differentially-regulated gene nucleic acid in operable linkage with the expression control sequence can also be referred to as a construct or transgene.

Any expression control sequence can be used depending on the purpose. For instance, if selective expression is desired, then expression control sequences which limit its expression can be selected. These include, e.g., tissue or cell-specific promoters, introns, enhancers, etc. For various methods of cell and tissue-specific expression, see, e.g., U.S. Pat.

Nos. 6,215,040, 6,210,736, and 6,153,427. These also include the endogenous promoter, i.e., the coding sequence can be operably linked to its own promoter. Inducible and regulatable promoters can also be utilized.

The present invention also relates to a transgenic animal which contains a functionally disrupted and a transgene stably integrated into the animals genome. Such an animal can be constructed using combinations any of the above- and below-mentioned methods. Such animals have any of the aforementioned uses, including permitting the knock-out of the normal gene and its replacement with a mutated gene. Such a transgene can be integrated at the endogenous gene locus so that the functional disruption and "knock-in" are carried out in the same step.

In addition to the methods mentioned above, transgenic animals can be prepared according to known methods, including, e.g., by pronuclear injection of recombinant genes into pronuclei of 1-cell embryos, incorporating an artificial yeast chromosome into embryonic stem cells, gene targeting methods, embryonic stem cell methodology, cloning methods, nuclear transfer methods. See, also, e.g., U.S. Patent Nos. 4,736,866; 4,873,191; 4,873,316; 5,082,779; 5,304,489; 5,174,986; 5,175,384; 5,175,385; 5,221,778; Gordon et al., Proc. Natl. Acad. Sci., 77:7380-7384, 1980; Palmiter et al., Cell, 41:343-345, 1985; Palmiter et al., Ann. Rev. Genet., 20:465-499, 1986; Askew et al., Mol. Cell. Bio., 13:4115-4124, 1993; Games et al. Nature, 373:523-527, 1995; Valancius and Smithies, Mol. Cell. Bio., 11:1402-1408, 1991; Stacey et al., Mol. Cell. Bio., 14:1009-1016, 1994; Hasty et al., Nature, 350:243-246, 1995; Rubinstein et al., Nucl. Acid Res., 21:2613-2617,1993; Cibelli et al., Science, 280:1256-1258, 1998. For guidance on recombinase excision systems, see, e.g., U.S. Pat. Nos. 5,626,159, 5,527,695, and 5,434,066. See also, Orban, P.C., et al., "Tissue- and Site-Specific DNA Recombination in Transgenic Mice," Proc. Natl. Acad. Sci. USA, 89:6861-6865 (1992); O'Gorman, S., et al., "Recombinase-Mediated Gene Activation and Site-Specific Integration in Mammalian Cells," Science, 251:1351-1355 (1991); Sauer, B., et al., "Cre-stimulated recombination at loxP-Containing DNA sequences placed into the mammalian genome," Polynucleotides Research, 17(1):147-161 (1989); Gagneten, S. et al. (1997) Nucl. Acids Res. 25:3326-3331; Xiao and Weaver (1997) Nucl. Acids Res. 25:2985-2991; Agah, R. et al. (1997) J. Clin. Invest. 100:169-179; Barlow, C. et al. (1997) Nucl. Acids Res. 25:2543-2545; Araki, K. et al. (1997) Nucl. Acids Res. 25:868-872; Mortensen, R. N. et al. (1992) Mol. Cell. Biol. 12:2391-2395 (G418 escalation method); Lakhlani, P. P. et al. (1997) Proc. Natl. Acad. Sci. USA 94:9950-9955 ("hit and run"); Westphal and Leder

(1997) Curr. Biol. 7:530-533 (transposon-generated "knock-out" and "knock-in"); Templeton, N. S. et al. (1997) Gene Ther. 4:700-709 (methods for efficient gene targeting, allowing for a high frequency of homologous recombination events, e.g., without selectable markers); PCT International Publication WO 93/22443 (functionally-disrupted).

A polynucleotide according to the present invention can be introduced into any non-human animal, including a non-human mammal, mouse (Hogan et al., Manipulating the Mouse Embryo: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1986), pig (Hammer et al., Nature, 315:343-345, 1985), sheep (Hammer et al., Nature, 315:343-345, 1985), cattle, rat, or primate. See also, e.g., Church, 1987, Trends in Biotech. 5:13-19; Clark et al., Trends in Biotech. 5:20-24, 1987); and DePamphilis et al., BioTechniques, 6:662-680, 1988. Transgenic animals can be produced by the methods described in U.S. Pat. No. 5,994,618, and utilized for any of the utilities described therein.

Database

The present invention also relates to electronic forms of polynucleotides, polypeptides, etc., of the present invention, including computer-readable medium (e.g., magnetic, optical, etc., stored in any suitable format, such as flat files or hierarchical files) which comprise such sequences, or fragments thereof, e-commerce-related means, etc. Along these lines, the present invention relates to methods of retrieving gene sequences from a computer-readable medium, comprising, one or more of the following steps in any effective order, e.g., selecting a cell or gene expression profile, e.g., a profile that specifies that said gene is differentially expressed in prostate cancer, and retrieving said differentially expressed gene sequences, where the gene sequences consist of the genes represented by Tables 1 and 2.

A "gene expression profile" means the list of tissues, cells, etc., in which a defined gene is expressed (i.e, transcribed and/or translated). A "cell expression profile" means the genes which are expressed in the particular cell type. The profile can be a list of the tissues in which the gene is expressed, but can include additional information as well, including level of expression (e.g., a quantity as compared or normalized to a control gene), and information on temporal (e.g., at what point in the cell-cycle or developmental program) and spatial expression. By the phrase "selecting a gene or cell expression profile," it is meant that a user decides what type of gene or cell expression pattern he is interested in retrieving, e.g., he may require that the gene is differentially expressed in a tissue, or he may require that the

gene is not expressed in blood, but must be expressed in prostate cancer. Any pattern of expression preferences may be selected. The selecting can be performed by any effective method. In general, "selecting" refers to the process in which a user forms a query that is used to search a database of gene expression profiles. The step of retrieving involves searching for results in a database that correspond to the query set forth in the selecting step. Any suitable algorithm can be utilized to perform the search query, including algorithms that look for matches, or that perform optimization between query and data. The database is information that has been stored in an appropriate storage medium, having a suitable computer-readable format. Once results are retrieved, they can be displayed in any suitable format, such as HTML.

For instance, the user may be interested in identifying genes that are differentially expressed in a prostate cancer. He may not care whether small amounts of expression occur in other tissues, as long as such genes are not expressed in peripheral blood lymphocytes. A query is formed by the user to retrieve the set of genes from the database having the desired gene or cell expression profile. Once the query is inputted into the system, a search algorithm is used to interrogate the database, and retrieve results.

Advertising, licensing, etc., methods

The present invention also relates to methods of advertising, licensing, selling, purchasing, brokering, etc., genes, polynucleotides, specific-binding partners, antibodies, etc., of the present invention. Methods can comprises, e.g., displaying a a differentially-regulated gene gene, a differentially-regulated gene polypeptide, or antibody specific for a differentially-regulated gene in a printed or computer-readable medium (e.g., on the Web or Internet), accepting an offer to purchase said gene, polypeptide, or antibody.

Other

A polynucleotide, probe, polypeptide, antibody, specific-binding partner, etc., according to the present invention can be isolated. The term "isolated" means that the material is in a form in which it is not found in its original environment or in nature, e.g., more concentrated, more purified, separated from component, etc. An isolated polynucleotide includes, e.g., a polynucleotide having the sequenced separated from the chromosomal DNA found in a living animal, e.g., as the complete gene, a transcript, or a cDNA. This polynucleotide can be part of a vector or inserted into a chromosome (by

specific gene-targeting or by random integration at a position other than its normal position) and still be isolated in that it is not in a form that is found in its natural environment. A polynucleotide, polypeptide, etc., of the present invention can also be substantially purified. By substantially purified, it is meant that polynucleotide or polypeptide is separated and is essentially free from other polynucleotides or polypeptides, i.e., the polynucleotide or polypeptide is the primary and active constituent. A polynucleotide can also be a recombinant molecule. By "recombinant," it is meant that the polynucleotide is an arrangement or form which does not occur in nature. For instance, a recombinant molecule comprising a promoter sequence would not encompass the naturally-occurring gene, but would include the promoter operably linked to a coding sequence not associated with it in nature, e.g., a reporter gene, or a truncation of the normal coding sequence.

The term "marker" is used herein to indicate a means for detecting or labeling a target. A marker can be a polynucleotide (usually referred to as a "probe"), polypeptide (e.g., an antibody conjugated to a detectable label), PNA, or any effective material.

The topic headings set forth above are meant as guidance where certain information can be found in the application, but are not intended to be the only source in the application where information on such topic can be found.

Reference materials

For other aspects of the polynucleotides, reference is made to standard textbooks of molecular biology. See, e.g., Hames et al., Polynucleotide Hybridization, IL Press, 1985; Davis et al., Basic Methods in Molecular Biology, Elsevir Sciences Publishing, Inc., New York, 1986; Sambrook et al., Molecular Cloning, CSH Press, 1989; Howe, Gene Cloning and Manipulation, Cambridge University Press, 1995; Ausubel et al., Current Protocols in Molecular Biology, John Wiley & Sons, Inc., 1994-1998.

The preceding description, utilize the present invention to its fullest extent. The preceding preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limiting the remainder of the disclosure in any way whatsoever. The entire disclosure of all applications, patents and publications, cited above and in the figures are hereby incorporated by reference in their entirety.

Claims:

1. A method for diagnosing a prostate cancer in a sample comprising prostate tissue, comprising:

determining the number of target genes which are differentially-regulated in said sample, wherein said target genes are selected from SEQ ID NO 1-211 of claim 26,

whereby said number is indicative of the probability that said sample comprises prostate cancer.

2. A method of claim 1, wherein said determining is performed by Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization using polynucleotide probes specific for genes selected from SEQ ID NO 1-211 of claim 26.

3. A method of claim 1, wherein said determining is performed by:

contacting said sample with a polynucleotide probe under conditions effective for said probe to hybridize specifically to a target nucleic acid in said sample, and

detecting the amount of hybridization between said probe and target nucleic acid, and

comparing the amount of hybridization in said sample with the amount of hybridization of said probe in a second sample comprising normal prostate tissue.

4. A method of claim 1, wherein said determining is performed by:

contacting said sample with a polynucleotide probe under conditions effective for said probe to hybridize specifically to a target nucleic acid in said sample, and

detecting the amount of hybridization between said probe and target nucleic acid, and

comparing the amount of hybridization in said sample with the amount of hybridization between a second probe and its corresponding second target nucleic acid in said sample.

5. A method of clam 2, wherein said probe is a contiguous sequence of at least 8 nucleotides selected from a polynucleotide sequence selected from SEQ ID NOS 1-107 of claim 26, or a complement thereto.

6. A method of assessing a therapeutic or preventative intervention in a subject having a prostate cancer, comprising,

determining the expression levels in a sample comprising prostate tissue of target genes which are differentially-regulated in prostate cancer,

wherein said target genes are selected from SEQ ID NO 1-211 of claim 26.

7. A method of claim 6, wherein the expression levels of at least 10 genes are determined.

8. A method of claim 6, wherein the determining is performed by Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization using polynucleotide probes specific for genes selected from SEQ IDS NO 1-211 of claim 26.

9. A method for identifying agents that modulate the expression of target polynucleotides differentially-regulated in prostate cancer cells, comprising,

contacting a prostate cell population with a test agent under conditions effective for said test agent to modulate the expression of a target polynucleotide in said cell population, and

determining whether said test agent modulates said target polynucleotide expression, wherein said target polynucleotide is selected from SEQ ID NOS 1-107 of claim 26.

10. A method of claim 9, wherein said agent is an antisense polynucleotide to said target polynucleotide sequence and which is effective to inhibit translation of said target polynucleotide.

11. A method for identifying agents that modulate a biological activity of a polypeptide differentially-regulated in prostate cancer cells, comprising,

contacting a polypeptide differentially-regulated in prostate cancer cells with a test agent under conditions effective for said test agent to modulate a biological activity of said polypeptide, and

determining whether said test agent modulates said biological activity, wherein said polypeptide is selected from SEQ ID NOS 108-211 of claim 26.

12. A method of treating prostate cancer, comprising,

administering to a subject in need thereof a therapeutic agent which is effective for regulating expression of at least one sequence selected from SEQ ID NOS 1-211 of claim 26.

13. A method of claim 12, wherein said agent is an antibody or an antisense which is effective to inhibit translation of said gene.

14. A method of diagnosing a prostate cancer comprising:

assessing the expression of at least one gene selected from SEQ ID NO 1-211 of claim 26, wherein said gene is differentially-regulated in said cancer.

15. A method of claim 14, wherein assessing is:

measuring mRNA expression levels of said or measuring the expression levels of polypeptide coded for by said gene.

16. A method of claim 14, further comprising:

comparing said expression to the expression of said polynucleotide in a known normal tissue.

17. A method of claim 14, wherein said assessing detecting is performed by: Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization, and

using a polynucleotide probe specific for a polynucleotide sequence selected from SEQ ID NOS 1-107 of claim 26.

18. A method of claim 14, wherein the expression of at least one up-regulated polynucleotide and at least one down-regulated polynucleotide are assessed.

19. A method of claim 14, wherein the expression of at least five up-regulated polynucleotides and at least five down-regulated polynucleotides are assessed.

20. A method of retrieving prostate cancer differentially-regulated gene sequences from a computer-readable medium, comprising:

selecting a gene expression profile that specifies that said gene is differentially-regulated in a prostate cancer, and retrieving prostate cancer differentially-regulated gene sequences,

where the gene sequences consist of genes selected from SEQ ID NO 1-211 of claim 26.

21. An ordered array of polynucleotide probes for detecting the expression of differentially-regulated prostate cancer genes in a sample, comprising:

polynucleotide probes associated with a solid support, wherein each probe is specific for a different differentially-regulated prostate cancer gene, and the probes are specific for genes selected from SEQ ID NO 1-211 of claim 26.

22. An array of claim 21, wherein said array comprises probes specific for up-regulated and down-regulated polynucleotides.

23. A method of advertising for sale, commercial use, or licensing, comprising:

displaying at least one polynucleotide or polypeptide sequence selected from

SEQ ID NO 1-211 of claim 26, or a complement thereto.

24. A non-human, transgenic mammal having a functional disruption in at least one gene selected from SEQ ID NO 1-211 of claim 26, and which is susceptible to prostate cancer.

25. A cell expression profile consisting of the expression pattern of a prostate cancer tissue sample for differentially-regulated genes of claim 26.

26. A plurality of genes which are differentially regulated in a prostate cancer, selected from:

up-regulated genes having SEQ ID NOS 1-75 and 140-211; and

down-regulated genes having SEQ ID 76-107 and 108-139.

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Table 1

DNA SEQ ID	Prt SEQ ID	Identifier	Exp	GI#	Gene Name and Description
1	140	PC030931U	U	337504	HUMRPS24A Human ribosomal protein S24 mRNA
2	141	PC010849U	U	3978243	AF070674 Homo sapiens inhibitor of apoptosis protein-1 (MIHC) mRNA complete cds
3	142	PC010839U	U	6912451	NM_012289.1| Homo sapiens Kelch-like ECH-associated protein 1 (KIAA0132),
4	143	PC010957U	U	4557844	NM_001034.1| Homo sapiens ribonucleotide reductase M2 polypeptide (RRM2) mRNA
5	144	PC020728U	U	4503478	NM_001960.1| Homo sapiens eukaryotic translation elongation factor 1 delta
6	145	PC021342U	U	340057	HUMUB Human poly-ubiquitin mRNA complete cds
7	146	PC030732U	U	4504374	Homo sapiens H factor 1 (complement) (HF1) mRNA
8		PC011348U	U	3093338	HSY17176 Homo sapiens mRNA from HIV-associated non-Hodgkin's lymphoma (clone hl2-264)
9	147	PC041029U	U	4589595	AB023193 Homo sapiens mRNA for KIAA0976 protein complete cds
10	148	PC040972U	U	4885132	Homo sapiens centromere protein F (400kD) (CENPF) mRNA
11	149	PC050853U	U	4503724	NM_000801.1| Homo sapiens FK506-binding protein 1A (12kD) (FKBP1A) mRNA
12	150	PC040158U	U	4826949	Homo sapiens kallikrein 7 (chymotryptic stratum corneum) (KLK7) mRNA
13	151	PC040441U	U	4826879	Homo sapiens oxidase (cytochrome c) assembly 1-like (OXA1L) mRNA
14	152	PC051210U	U	4506056	NM_002731.1| Homo sapiens protein kinase, cAMP-dependent, catalytic, beta
15	154	PC050296U	U	5453633	Homo sapiens dynein cytoplasmic light intermediate polypeptide 2 (DNCLI2) mRNA
16	155	PC050151U	U	6715599	NM_002078.2| Homo sapiens golgi autoantigen, golgin subfamily a, 4
17	156	PC050149U	U	2217930	AB004884 Homo sapiens mRNA for PKU-alpha,
18	157	PC052095U	U	641957	HUMMYOHCB Human nonmuscle myosin heavy chain-B (MYH10) mRNA partial cds
19	158	PC052029U	U	5803218	Homo sapiens serine protease inhibitor Kazal type 5 (SPINK5) mRNA
20	159	PC050620U	U	4504580	NM_003641.1| Homo sapiens interferon induced transmembrane protein 1, (IFITM1), mRNA
21	160	PC041338U	U	8051620	Homo sapiens 2'5'-oligoadenylate synthetase 1 (OAS1) transcript variant E18 mRNA
22	161	PC041980U	U	6735451	HSA271091 Homo sapiens mRNA for B-ind1 protein (B-ind1 gene)
23	162	PC060474U	U	4759321	Homo sapiens wingless-type MMTV integration site family member 2B (WNT2B) mRNA
24	163	PC060443U	U	4506730	Homo sapiens ribosomal protein S6 (RPS6) mRNA
25	164	PC060441U	U	1688257	HSU78045 Human collagenase and stromelysin genes, complete cds, and metalloelastase gene, partial cds
26	165	PC070152U	U	4506712	Homo sapiens ribosomal protein S27a (RPS27A) mRNA
27	166	PC060529U	U	4503820	Homo sapiens FYN-binding protein (FYB-120130) (FYB) mRNA and translated products
28	167	PC080348U	U	9623360	AF261688 Homo sapiens DNA polymerase epsilon p12 subunit gene, complete cds
29	168	PC070544U	U	1679960	S42658 S3 ribosomal protein [human colon mRNA 826 nt]
30	169	PC070343U	U	4507210	Homo sapiens signal recognition particle 14kD (homologous Alu RNA-binding protein) (SRP14) mRNA
31	170	PC061477U	U	4506386	Homo sapiens RAD23 (S. cerevisiae) homolog B (RAD23B) mRNA
32	171	PC060940U	U	5052074	Homo sapiens PAPS synthetase-2 (PAPSS2) mRNA
33	172	PC061779U	U	4504766	Homo sapiens integrin beta 1 (fibronectin receptor beta polypeptide antigen CD29 includes MDF2 MSK12) (ITGB1) mRNA
34	173	PC061839U	U	8394498	Homo sapiens ubiquitin associated protein (UBAP) mRNA
35	174	PC061827U	U	7382495	Homo sapiens p21Cdc42Rac1-activated kinase 1 (yeast Ste20-related) (PAK1) mRNA
36	175	PC080511U	U	4504190	NM_000179.1| Homo sapiens mutS (E. coli) homolog 6 (MSH6),
37	176	PC090754U	U	4503472	Homo sapiens eukaryotic translation elongation factor 1 alpha 1-like 14 (EEF1A1L14) mRNA
38	177	PC090842U	U	4557031	Homo sapiens lactate dehydrogenase B (LDHB) mRNA
39	178	PC091028U	U	7662425	Homo sapiens KIAA0976 protein (KIAA0976) mRNA
40		PC070890U	U	6531675	AF205588.1|AF205588 Homo sapiens ZNF01 and HUMORFKG1B genes
41		PC071851U	U	3090894	AF052497 Homo sapiens clone B18 unknown mRNA
42	179	PC070729U	U	8923790	Homo sapiens rTS beta protein (HSRTSBETA) mRNA

Table 1

43	180	PC080742U	U	4507186	NM_003125.1| Homo sapiens small proline-rich protein 1B (cornifin)
44	181	PC100113U	U	6647292	AF166330.2|AF166330 Homo sapiens stratum corneum chymotryptic enzyme gene
45		PC100356U	U	3093334	HSY17172 Homo sapiens mRNA from HIV-associated non-Hodgkin's lymphoma (clone hl2-22)
46	182	PC100428U	U	4502980	NM_001861.1| Homo sapiens cytochrome c oxidase subunit IV (COX4),
47	183	PC090230U	U	3252910	AF056322 Homo sapiens SP100-HMG nuclear autoantigen (SP100) mRNA complete cds
48	184	PC090233U	U	4504192	Homo sapiens general transcription factor IIB (GTF2B) mRNA
49	185	PC101863U	U	35037	HSNFIV H.sapiens mRNA for nuclear factor IV
50	186	PC090625U	U	7706215	Homo sapiens H-2K binding factor-2 (LOC51580) mRNA
51	187	PC101430U	U	609453	M69199.1|HUMG0S2A Human G0S2 protein gene, complete cds
52	188	PC091425U	U	4732025	AF118569 Homo sapiens angiotensin I converting enzyme precursor
53	189	PC010434U	U	4505374	NM_002499.1| Homo sapiens neogenin (chicken) homolog 1
54	190	PC010139U	U	7657203	Homo sapiens acidic 82 kDa protein mRNA (HSU15552) mRNA
55	191	PC010337U	U	6005813	Homo sapiens serine threonine protein kinase (NDR) mRNA
56	192	PC010336U	U	7662579	Homo sapiens PRO0644 protein (PRO0644) mRNA
57	193	PC020185U	U	7669502	NM_013995.1| Homo sapiens lysosomal-associated membrane protein 2
58	194	PC020162U	U	4507164	NM_003113.1| Homo sapiens nuclear antigen Sp100 (SP100) mRNA
59	195	PC030247U	U	348706	HUMCACTHBS Homo sapiens cathepsin B mRNA 3' UTR with a stem-loop structure providing mRNA stability
60	196	PC030471U	U	31396	HSFIB1 Human mRNA for fibronectin (FN precursor)
61	197	PC030454U	U	4506678	Homo sapiens ribosomal protein S10 (RPS10) mRNA
62	198	PC030326U	U	4507148	Homo sapiens superoxide dismutase 1 soluble (amyotrophic lateral sclerosis 1 (adult)) (SOD1) mRNA
63	199	PC030425U	U	415818	HSMKI67 H.sapiens mki67a mRNA (long type) for antigen of monoclonal antibody Ki-67
64	200	PC091527U	U	5803091	Homo sapiens methionine aminopeptidase; eIF-2-associated p67 (MNPEP) mRNA
65	201	PC092004U	U	8922823	NM_018300.1| Homo sapiens hypothetical protein FLJ11015 (FLJ11015)
66	202	PC091888U	U	4757809	Homo sap/ ATP synthase H+ transporting mito.F1 complex alpha subunit isoform 1 cardiac muscle (ATP5A1) nuclear gene
67	203	PC091853U	U	31091	X16869.1|HSEF1AC Human mRNA for elongation factor 1-alpha
68	204	PC092052U	U	4505634	Homo sapiens BH-protocadherin (brain-heart) (9999DH7) mRNA
69	205	PC091839U	U	7188646	AF222043 Homo sapiens ubiquitin-associated protein (NAG20) mRNA complete cds
70	206	PC111181U	U	7416940	AF139077 Homo sapiens MS-14 mRNA complete cds
71	207	PC111168U	U	4759283	NM_004181.1| Homo sapiens ubiquitin carboxyl-terminal esterase L1
72	208	PC120136U	U	7706728	Homo sapiens TBX3-iso protein (TBX3-iso) mRNA
73	209	PC120331U	U	4504424	NM_002128.1| Homo sapiens high-mobility group (nonhistone chromosomal) protein 1
74	210	PC121671U	U	7661635	Homo sapiens DKFZP564O2082 protein (DKFZP564O2082) mRNA
75	211	PC020741U	U	7657824	NM_014393.1| Homo sapiens staufen (Drosophila, RNA-binding protein) homolog 2
	153	PC051231U	U	4506600	Homo sapiens ribosomal protein L14 (RPL14) mRNA
		PC020627U	U	8923949	Homo sapiens ovarian cancer related protein OVN9-3 (OVN9-3) mRNA
		PC110927U	U	8923282	NM_017754.1| Homo sapiens hypothetical protein FLJ20302 (FLJ20302

Table 2

DNA SEQ ID	Prt SEQ ID	Identifier	Exp	GI#	Gene Name and Description
76	108	PC040734D	D	5174656	NM_006096.1| Homo sapiens differentiation-related gene 1 nickel-specific induction protein
77	109	PC040156D	D	4505748	Homo sapiens phosphofructokinase muscle (PFKM) mRNA
78	110	PC051745D	D	4758751	Homo sapiens neuronal apoptosis inhibitory protein (NAIP) mRNA
79	111	PC042021D	D	4505986	Homo sapiens PTPRF interacting protein binding protein 1 (liprin beta 1) (PPFIBP1) mRNA and translated products
80	112	PC060144D	D	4758199	NM_004415.1| Homo sapiens desmoplakin (DPI, DPII) (DSP) mRNA
81	113	PC080139D	D	7657159	NM_014362.1| Homo sapiens 3-hydroxyisobutyryl-Coenzyme A hydrolase (HIBCH), mRNA
82	114	PC080435D	D	4758807	Homo sapiens ras GTPase activating protein-like (NGAP) mRNA
83	115	PC070436D	D	9790904	NM_001924.1| Homo sapiens growth arrest and DNA-damage-inducible
84	116	PC061342D	D	186485	HUMINT04 Human leukocyte adhesion protein p15095 alpha subunit gene exons 16 - 21
85	117	PC060793D	D	4507582	NM_000043.1| Homo sapiens tumor necrosis factor receptor superfamily
86	118	PC060743D	D	4557256	Homo sapiens adenylate cyclase 8 (brain) (ADCY8) mRNA
87	119	PC061528D	D	4506700	Homo sapiens ribosomal protein S23 (RPS23) mRNA
88	120	PC090788D	D	5031638	Homo sapiens cornichon-like (CNIL) mRNA
89	121	PC090722D	D	7670747	AF227906 Homo sapiens UDP-glucoseglycoprotein glucosyltransferase 2 precursor mRNA complete cds
90	122	PC071770D	D	31441	HSFNRB Human mRNA for integrin beta 1 subunit
91	123	PC090677D	D	187701	HUMMHBA123 Human MHC protein homologous to chicken B complex protein mRNA complete cds
92	124	PC101847D	D	5902021	Homo sapiens PL6 protein (PL6) mRNA
93	125	PC090622D	D	4506858	NM_002997.1| Homo sapiens syndecan 1 (SDC1) mRNA
94	126	PC010433D	D	4827043	Homo sapiens thyroid hormone receptor-associated protein 240 kDa subunit (TRAP240) mRNA
95	127	PC020238D	D	4503090	NM_001893.1| Homo sapiens casein kinase 1, delta (CSNK1D) mRNA
96	128	PC030301D	D	4506728	Homo sapiens ribosomal protein S5 (RPS5) mRNA
97	129	PC110249D	D	4759257	Homo sapiens Ac-like transposable element (ALTE) mRNA
98	130	PC110541D	D	5031778	Homo sapiens interferon gamma-inducible protein 16 (IFI16) mRNA
99		PC110431D	D	3885367	AB019564 Homo sapiens mRNA expressed only in placental villi clone SMAP47
100	131	PC110940D	D	4758949	NM_000942.1| Homo sapiens peptidylprolyl isomerase B (cyclophilin B)
101	132	PC111588D	D	4503412	Homo sapiens diphtheria toxin receptor (heparin-binding epidermal growth factor-like growth factor) (DTR) mRNA
102	133	PC111669D	D	7705822	Homo sapiens N-terminal acetyltransferase complex ard1 subunit (LOC51126) mRNA
103	134	PC032046D	D	7657325	NM_014623.1| Homo sapiens male-enhanced antigen (MEA),
104	135	PC120741D	D	5174388	NM_005891.1| Homo sapiens acetyl-Coenzyme A acetyltransferase 2
105	136	PC120740D	D	311380	HSTCP1 Human t-complex polypeptide 1 gene
106	137	PC010353D	D	4506660	Homo sapiens ribosomal protein L7a (RPL7A) mRNA
107	139	PC030968D	D	4507668	Homo sapiens tumor protein translationally-controlled 1 (TPT1) mRNA
	138	PC031146D	D	8924228	NM_018636.1| Homo sapiens hypothetical protein PRO2987 (PRO2987)

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Table 3

Name	Serial No.	Expression	Protein GI#	Classification	Domain	Domain description	Score	E	seq-f	seq-t		
PC340	PC010139U	U	7657204		Homo sapiens acidic 82 kDa protein mRNA (HSU15552) mRNA [redacted]							
	PC010139U	U	7657204		Ribosomal_L2	Ribosomal Proteins L2	3.6	2.70E-01	197	217		
PC342	PC010336U	U	7662580		Homo sapiens PRO0644 protein (PRO0644) mRNA [redacted]							
	PC010336U	U	7662580									
PC341	PC010337U	U	6005814		Homo sapiens serine/threonine protein kinase (NDR) mRNA [redacted]							
	PC010337U	U	6005814		pkinase	Protein kinase domain	221.1	8.30E-64	89	359		
PC330	PC010433D	D	4827044	Down-regulated	Homo sapiens thyroid hormone receptor-associated protein, 240 kDa subunit (TRAP240) mRNA [redacted]							
	PC010433D	D	4827044		Na_K-ATPase	Sodium / potassium ATPase beta chain	2.5	3.50E-01	224	239		
	PC010433D	D	4827044		Chal_sti1_synt_C	Chalcone and stilbene synthases, C-te	2.7	7.00E-01	1735	1752		
	PC010433D	D	4827044		A_deamin	Adenosine-deaminase (editase) domain	1.2	9.10E-01	140	148		
PC329	PC010434U	U	4505375		NM_002499.1|Homo sapiens neogenin (chicken) homolog 1 [redacted]							
	PC010434U	U	4505375		fn3	Fibronectin type III domain	367.4	7.70E-108	954	1044		
	PC010434U	U	4505375		ig	Immunoglobulin domain	131.9	1.20E-40	355	412		
	PC010434U	U	4505375		Ribosomal_L23	Ribosomal protein L23	2.9	9.40E-01	662	676		
PC007	PC010839U	U	6912452		NM_012289.1|Homo sapiens Kelch-like ECH-associated protein 1 (KIAA0132) [redacted]							
	PC010839U	U	6912452		Kelch	Kelch motif	271.7	5.10E-79	553	598		
	PC010839U	U	6912452		BTB	BTB/POZ domain	100.8	1.40E-27	61	179		
	PC010839U	U	6912452		PI3K_p85B	PI3-kinase family, p85-binding domain	-21.1	8.20E-01	176	238		
PC006	PC010849U	U	3978244		AF070674|Homo sapiens inhibitor of apoptosis protein 1 (MIHG) mRNA, complete cds [redacted]							
	PC010849U	U	3978244		BIR	Inhibitor of Apoptosis domain	395.2	3.30E-116	258	323		
	PC010849U	U	3978244		CARD	Caspase recruitment domain	125.1	6.80E-35	440	529		
	PC010849U	U	3978244		zf-C3HC4	Zinc finger, C3HC4 type (RING finger)	22.1	8.50E-07	557	591		
	PC010849U	U	3978244		zf-C4	Zinc finger, C4 type (two domains)	3	7.40E-01	555	563		
PC505	PC010853D	D	4506661	Down-regulated	Homo sapiens ribosomal protein L7a (RPL7A) mRNA [redacted]							
	PC010853D	D	4506661		Ribosomal_L7Ae	Ribosomal protein L7Ae/L30e/S12e/Gad	103.9	1.60E-28	122	216		
	PC010853D	D	4506661		Ribosomal_L39	Ribosomal L39 protein	-8.6	2.60E-01	211	244		
PC013	PC010957U	U	4557845		NM_001034.1|Homo sapiens ribonucleotide reductase M2 polypeptide (RRM2) mRNA [redacted]							
	PC010957U	U	4557845		ribonuc_red_sm	Ribonucleotide reductase, small chain	598.8	1.70E-177	70	351		
PC042	PC011348U	U	12005805		HSY17176|Homo sapiens mRNA from HIV associated non-Hodgkin's lymphoma (clone hl2-264) [redacted]							
	PC011348U	U	12005805		oxidored_q1	NADH-Ubiquinone/plastoquinone (com	22.9	9.30E-07	82	108		
PC353	PC020162U	U	4507165		NM_003113.1|Homo sapiens nuclear antigen Sp100 (SP100) mRNA [redacted]							
	PC020162U	U	4507165									
PC350	PC020185U	U	7669503		NM_013995.1|Homo sapiens lysosomal-associated membrane protein 2 [redacted]							
	PC020185U	U	7669503		Lamp	Lysosome-associated membrane glycopr	767.3	3.20E-228	44	410		
PC358	PC020238D	D	4503091	Down-regulated	NM_001893.1|Homo sapiens casein kinase 1, delta (CSNK1D) mRNA [redacted]							
	PC020238D	D	4503091		pkinase	Protein kinase domain	146.4	2.60E-41	9	239		
PC367	PC020627U	U	14424570		Homo sapiens, clone MGC:16614 IMAGE:3834 [redacted]							
	PC020627U	U	14424570									
PC022	PC020728U	U	4503479		NM_001960.1|Homo sapiens eukaryotic translation elongation factor 1 delta [redacted]							
	PC020728U	U	4503479		EF1BD	EF-1 guanine nucleotide exchange doma	189.4	3.00E-54	195	281		
	PC020728U	U	4503479		bZIP	bZIP transcription factor	10.1	1.30E-02	79	114		
PC517	PC020741U	U	7657625		NM_014393.1|Homo sapiens staufen (Drosophila, RNA-binding protein) homolog 2 [redacted]							
	PC020741U	U	7657625		dsrm	Double-stranded RNA binding motif	175.1	6.10E-50	276	341		

Table 3

PC031	PC021342U	U	340058		HUMUB|Human poly-ubiquitin mRNA, complete cds [redacted]							
	PC021342U	U	340058		ubiquitin	Ubiquitin family	529.9	9.20E-157	193	266		
PC374	PC030247U	U	291888		HUMCATHBS|Homo sapiens cathepsin B mRNA 3'UTR with a stem-loop structure providing mRNA stabili [redacted]							
	PC030247U	U	291888		Peptidase_C1	Papain family cysteine protease	393.5	6.50E-119	80	329		
	PC030247U	U	291888		Metallothio_2	Metallothionein	-36.1	7.50E-01	139	200		
PC383	PC030301D	D	4506729	Down-regulated	Homo sapiens ribosomal protein S5 (RPS5) mRNA [redacted]							
	PC030301D	D	4506729		Ribosomal_S7	Ribosomal protein S7p/S5e	245.5	3.90E-71	51	204		
PC391	PC030326U	U	4507149		Homo sapiens superoxide dismutase 1, soluble (amyotrophic lateral sclerosis 1 (adult)) (SOD1) mRNA [redacted]							
	PC030326U	U	4507149		sodcu	Copper/zinc superoxide dismutase (SOD	339.5	2.50E-105	1	154		
PC392	PC030425U	U	415819		HSMKI67A|H.sapiens mki67a mRNA (long type) for antigen of monoclonal antibody Ki-67 [redacted]							
	PC030425U	U	415819		FHA	FHA domain	83.5	2.20E-22	27	91		
	PC030425U	U	415819		Peptidase_M10	Matrixin	-104.7	3.60E-01	1806	1923		
	PC030425U	U	415819		Sua5_yciO_yrdC	yrdC domain	-71	4.10E-01	2335	2475		
	PC030425U	U	415819		Ribosomal_S3_C	Ribosomal protein S3, C-terminal doma	2.5	7.30E-01	620	642		
	PC030425U	U	415819		HMG14_17	HMG14 and HMG17	-12.8	9.10E-01	106	186		
PC386	PC030454U	U	4506679		Homo sapiens ribosomal protein S10 (RPS10) mRNA [redacted]							
	PC030454U	U	4506679									
PC384	PC030471U	U	31397		HSFIB1|Human mRNA for fibronectin (FN precursor) [redacted]							
	PC030471U	U	31397		fn3	Fibronectin type III domain	1202.8	0.00E+00	2046	2123		
	PC030471U	U	31397		fn1	Fibronectin type I domain	840	4.20E-250	2237	2272		
	PC030471U	U	31397		fn2	Fibronectin type II domain	194.4	1.60E-74	393	434		
	PC030471U	U	31397		CXCXC	CXCXC repeat	5.7	6.30E-01	2251	2264		
	PC030471U	U	31397		vwc	von Willebrand factor type C domain	-16.7	7.80E-01	2237	2313		
PC033	PC030732U	U	4504375		Homo sapiens H factor 1 (complement) (HF1) mRNA [redacted]							
	PC030732U	U	4504375		sushi	Sushi domain (SCR repeat)	1149.3	0.00E+00	1167	1228		
PC003	PC030931U	U	337506		HUMRPS24A|Human ribosomal protein S24 mRNA [redacted]							
	PC030931U	U	337506		Ribosomal_S24e	Ribosomal protein S24e	194	1.20E-55	23	105		
PC511	PC030968D	D	4507669	Down-regulated	Homo sapiens tumor protein, translationally-controlled 1 (TPT1) mRNA [redacted]							
	PC030968D	D	4507669		TCTP	Translationally controlled tumor prot	375.5	2.80E-110	1	169		
	PC030968D	D	4507669		MethyltransfD12	D12 class N6 adenine-specific DNA met	3.5	3.00E-01	74	99		
PC508	PC031146D	D	7959937	Down-regulated	Homo sapiens PRO2987 mRNA, complete cds [redacted]							
	PC031146D	D	7959937									
PC468	PC032046D	D	7657326	Down-regulated	NM_014623.1|Homo sapiens male-enhanced antigen (MEA) [redacted]							
	PC032046D	D	7657326									
PC64	PC040156D	D	4505749	Down-regulated	Homo sapiens phosphofructokinase, muscle (PFKM) mRNA [redacted]							
	PC040156D	D	4505749		PFK	Phosphofructokinase	929.6	0.00E+00	402	689		
PC062	PC040158U	U	4826950		Homo sapiens kallikrein 7 (chymotryptic, stratum corneum) (KLK7) mRNA [redacted]							
	PC040158U	U	4826950		trypsin	Trypsin	277	1.90E-88	30	245		
	PC040158U	U	4826950		toxin_4	Anenome neurotoxin	-3.3	4.70E-01	200	239		
PC068	PC040441U	U	4826880		Homo sapiens oxidase (cytochrome c) assembly 1-like (OXA1L) mRNA [redacted]							
	PC040441U	U	4826880		60KD_IMP	60Kd inner membrane protein	-2.6	4.30E-10	199	398		
PC51	PC040734D	D	5174657	Down-regulated	NM_006096.1|Homo sapiens differentiation-related gene 1 (nickel-specific induction protein) [redacted]							
	PC040734D	D	5174657		Ndr	Ndr family	716	8.80E-213	24	366		
	PC040734D	D	5174657		abhydrolase	alpha/beta hydrolase fold	10.3	1.90E-03	89	309		

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Table 3

PC059	PC040972U	U	4885133		Homo sapiens centromere protein E (400kD) (CENPE) mRNA		[redacted]					
	PC040972U	U	4885133		bZIP	bZIP transcription factor	68.1	4.80E-19	2930	2962		
	PC040972U	U	4885133		M	M protein repeat	29.7	3.50E-06	2972	2992		
	PC040972U	U	4885133		KID_repeat	KID repeat	26.6	3.10E-05	2938	2948		
	PC040972U	U	4885133		filament	Intermediate filament protein	13.2	8.80E-04	2810	2833		
	PC040972U	U	4885133		Trp_repressor	Trp repressor protein	-16.9	5.50E-02	1065	1157		
	PC040972U	U	4885133		RNA_pol_L	RNA polymerases L / 13 to 16 kDa subu	-28.7	9.90E-02	840	923		
	PC040972U	U	4885133		Myosin_tail	Myosin tail	4.3	1.40E-01	2283	2338		
	PC040972U	U	4885133		DUF164	Uncharacterized ACR, COG1579	-91.7	1.30E-01	2560	2797		
	PC040972U	U	4885133		HALZ	Homeobox associated leucine zipper	9	1.80E-01	2885	2928		
	PC040972U	U	4885133		OSCP	ATP synthase delta (OSCP) subunit	4.1	2.10E-01	2283	2294		
	PC040972U	U	4885133		K-box	K-box region	-40.4	3.10E-01	2440	2524		
	PC040972U	U	4885133		HlyD	HlyD family secretion protein	-60.5	3.30E-01	2461	2730		
	PC040972U	U	4885133		DUF38	Domain of unknown function DUF38	3.9	4.00E-01	1888	1914		
	PC040972U	U	4885133		dynamin_2	Dynamin central region	-179.4	4.20E-01	991	1223		
	PC040972U	U	4885133		HR1	Hr1 repeat motif	-4.4	4.70E-01	2201	2271		
	PC040972U	U	4885133		Apolipoprotein	Apolipoprotein A1/A4/E family	-118.2	4.90E-01	2295	2547		
	PC040972U	U	4885133		formyl_transf	Formyl transferase	3	5.60E-01	3068	3081		
	PC040972U	U	4885133		ERM	Ezrin/radixin/moesin family	-227.4	6.50E-01	2028	2290		
	PC040972U	U	4885133		Tropomyosin	Tropomyosin	1.3	7.20E-01	2418	2451		
	PC040972U	U	4885133		Borrelia_orfA	Borrelia ORF-A	-107.4	7.40E-01	417	744		
	PC040972U	U	4885133		PFEMP	Plasmodium falciparum erythrocyte men	-89.6	7.90E-01	2844	2950		
	PC040972U	U	4885133		BglG_antitermin	Transcriptional antiterminator bglG f	-41.4	8.40E-01	2891	2967		
	PC040972U	U	4885133		TFIIE_beta	TFIIE beta subunit core domain	-15.1	8.40E-01	566	624		
	PC040972U	U	4885133		TarH	Tar ligand binding domain homologue	-28.4	8.80E-01	2666	2793		
	PC040972U	U	4885133		FliD	Flagellar hook-associated protein 2	-252.1	9.10E-01	2261	2712		
PC057	PC041029U	U	4589596		Homo sapiens mRNA for KIAA0976 protein, complete cds		[redacted]					
	PC041029U	U	4589596		laminin_Nterm	Laminin N-terminal (Domain VI)	37	8.80E-14	50	295		
	PC041029U	U	4589596		laminin_EGF	Laminin EGF-like (Domains III and V)	31.8	8.00E-07	297	341		
	PC041029U	U	4589596		EGF	EGF-like domain	3.9	5.20E-01	299	326		
PC104	PC041338U	U	8051621		Homo sapiens 2'-5' oligoadenylate synthetase 1 (OAS1) transcript variant E18 mRNA		[redacted]					
	PC041338U	U	8051621		NTP_transf_2	Nucleotidyltransferase domain	0.3	4.10E-02	33	142		
PC112	PC041980U	U	6735452		HSA Homo sapiens mRNA for B and H protein (B and H gene)		[redacted]					
	PC041980U	U	6735452									
PC121	PC042021D	D	4505987	Down-regulated	Homo sapiens PTPRF interacting protein, binding protein 1 (liprin beta 1) (PPFIBP1) mRNA and translated products		[redacted]					
	PC042021D	D	4505987		SAM	SAM domain (Sterile alpha motif)	109.5	3.30E-30	711	774		
	PC042021D	D	4505987		integrase_DNA	DNA binding domain of tn916 integrase	28.1	1.10E-05	187	251		
	PC042021D	D	4505987		WHEP-TRS	WHEP-TRS domain	15.9	1.20E-04	123	137		
	PC042021D	D	4505987		DUF16	Protein of unknown function DUF16	-22.2	1.40E-01	90	167		
	PC042021D	D	4505987		bZIP	bZIP transcription factor	5.2	3.20E-01	205	244		
	PC042021D	D	4505987		STAT	STAT protein, all-alpha domain	-71.8	5.40E-01	2	162		
PC088	PC050149U	U	2217931		Homo sapiens mRNA for PKU-alpha		[redacted]					
	PC050149U	U	2217931		pkinase	Protein kinase domain	245.9	2.90E-71	409	688		
	PC050149U	U	2217931		A2M	Alpha-2-macroglobulin family	1.1	2.40E-01	471	493		

Table 3

	PC050149U	U	2217931		DUF164	Uncharacterized ACR, COG1579	-99.2	5.10E-01	356	574		
	PC050149U	U	2217931		Stathmin	Stathmin family	-22.4	8.40E-01	126	263		
PC087	PC050151U	U	6715600		NM_002078 Homo sapiens golgi autoantigen, golgin subfamily a		[redacted]					
	PC050151U	U	6715600		GRIP	GRIP domain	77.2	1.70E-20	2171	2215		
	PC050151U	U	6715600		M	M protein repeat	48.2	9.30E-12	2065	2085		
	PC050151U	U	6715600		Involucrin	Involucrin repeat	14	4.20E-02	2005	2014		
	PC050151U	U	6715600		Ribosomal_L29	Ribosomal L29 protein	-7.7	8.80E-02	1263	1325		
	PC050151U	U	6715600		DNA_topoisoIV	DNA gyrase/topoisomerase IV, subunit	3.1	1.00E-01	1850	1882		
	PC050151U	U	6715600		bZIP	bZIP transcription factor	6.7	1.20E-01	864	897		
	PC050151U	U	6715600		DUF164	Uncharacterized ACR, COG1579	-89.1	1.20E-01	1559	1775		
	PC050151U	U	6715600		Tropomyosin	Tropomyosin	3.4	1.50E-01	553	578		
	PC050151U	U	6715600		Lipoprotein_7	Adhesin lipoprotein	-123	2.20E-01	725	1177		
	PC050151U	U	6715600		DUF156	Uncharacterized BCR, COG1937	-9.6	3.90E-01	916	974		
	PC050151U	U	6715600		UVR	UvrB/uvrC motif	-3.8	5.00E-01	363	397		
	PC050151U	U	6715600		ATP-synt_ab_C	ATP synthase alpha/beta chain, C term	-21.2	5.10E-01	381	486		
	PC050151U	U	6715600		ICL	Isocitrate lyase family	-1.6	5.90E-01	1963	1980		
	PC050151U	U	6715600		CagE_TrbE_VirB	CagE, TrbE, VirB family, component of	-86.1	6.30E-01	1091	1290		
	PC050151U	U	6715600		Borrelia_orfA	Borrelia ORF-A	-107.4	7.40E-01	1366	1698		
	PC050151U	U	6715600		SEA	SEA domain	-10.6	7.80E-01	1177	1299		
	PC050151U	U	6715600		DUF28	Domain of unknown function DUF28	-167.8	8.00E-01	1248	1422		
	PC050151U	U	6715600		Bac_DNA_binding	Bacterial DNA-binding protein	3.4	8.20E-01	2103	2118		
	PC050151U	U	6715600		MSG	Major surface glycoprotein	-6.3	9.60E-01	1576	1635		
	PC050151U	U	6715600		Transposase_8	Transposase	-21.9	9.70E-01	1150	1228		
PC085	PC050296U	U	5453634		Homo sapiens dynein, cytoplasmic, light intermediate polypeptide 2 (DNCLI2) mRNA		[redacted]					
	PC050296U	U	5453634		GTP_CDC	Cell division protein	5.7	6.60E-02	56	71		
	PC050296U	U	5453634		ABC_tran	ABC transporter	-66	1.80E-01	54	291		
	PC050296U	U	5453634		SRP54	SRP54-type protein, GTPase domain	4.2	2.20E-01	53	74		
PC101	PC050620U	U	4504581		NM_003641 Homo sapiens interferon induced transmembrane protein 1 (IFITM1) mRNA		[redacted]					
	PC050620U	U	4504581									
PC060	PC050853U	U	4503725		NM_000801 Homo sapiens FK506-binding protein 1A (12kD) (FKBP1A) mRNA		[redacted]					
	PC050853U	U	4503725		FKBP	FKBP-type peptidyl-prolyl cis-trans isor	179.2	6.30E-55	11	105		
PC076	PC051210U	U	4506057		NM_002731 Homo sapiens protein kinase, cAMP-dependent, catalytic, beta		[redacted]					
	PC051210U	U	4506057		pkinase	Protein kinase domain	303.4	1.50E-88	44	298		
	PC051210U	U	4506057		pkinase_C	Protein kinase C terminal domain	27.4	1.90E-08	299	330		
PC083	PC051231U	U	4506601		Homo sapiens ribosomal protein L14 (RPL14) mRNA		[redacted]					
	PC051231U	U	4506601		Ribosomal_L14e	Ribosomal protein L14	120.1	2.20E-33	4	81		
	PC051231U	U	4506601		Ribosomal_L27e	Ribosomal L27e protein family	-62	1.60E-01	3	120		
PC90	PC051745D	D	4758752	Down-regulated	Homo sapiens neuronal apoptosis inhibitory protein (NAIP) mRNA		[redacted]					
	PC051745D	D	4758752		BIR	Inhibitor of Apoptosis domain	354.1	8.10E-104	281	346		
	PC051745D	D	4758752		AAA	ATPase family associated with various	-45.7	4.00E-01	465	658		
	PC051745D	D	4758752		Peptidase_M29	Thermophilic metalloprotease (M29)	-0.4	6.20E-01	957	964		
	PC051745D	D	4758752		ABC_tran	ABC transporter	-72.9	6.40E-01	463	602		
	PC051745D	D	4758752		NB-ARC	NB-ARC domain	1.5	7.70E-01	465	483		
PC100	PC052029U	U	5803219		Homo sapiens serine protease inhibitor, Kazal type 5 (SPINK5) mRNA		[redacted]					

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Table 3

	PC052029U	U	5803219		kazal	Kazal-type serine protease inhibitor	172.5	3.70E-49	993	1046		
	PC052029U	U	5803219		RNA_POL_M_15K	RNA polymerases M/15 Kd subunit	-7.8	6.40E-01	308	363		
	PC052029U	U	5803219		DnaJ_CXXCXGXG	DnaJ central domain (4 repeats)	-51.3	6.50E-01	751	323		
	PC052029U	U	5803219		Hirudin	Hirudin	-10.8	7.40E-01	380	441		
PC093	PC052095U	U	641958		HOMMYOHCB Human nonmuscle myosin heavy chain-B (MYH10) mRNA, partial cds [redacted]							
	PC052095U	U	641958		myosin_head	Myosin head (motor domain)	1495.3	0.00E+00	87	771		
	PC052095U	U	641958		Myosin_tail	Myosin tail	788.7	1.20E-234	1073	1931		
	PC052095U	U	641958		M	M protein repeat	76.1	3.70E-20	1898	1918		
	PC052095U	U	641958		Myosin_N	Myosin N-terminal SH3-like domain	70.1	2.40E-18	33	77		
	PC052095U	U	641958		IQ	IQ calmodulin-binding motif	22.3	5.90E-04	787	807		
	PC052095U	U	641958		Apolipoprotein	Apolipoprotein A1/A4/E family	-98.6	6.60E-02	1083	1318		
	PC052095U	U	641958		DUF164	Uncharacterized ACR, COG1579	-86.6	8.70E-02	1018	1250		
	PC052095U	U	641958		bZIP	bZIP transcription factor	7.2	8.80E-02	1788	1817		
	PC052095U	U	641958		Prismane	Prismane	-394.9	9.50E-02	171	425		
	PC052095U	U	641958		K-box	K-box region	-35.3	1.20E-01	965	1062		
	PC052095U	U	641958		Tub	Tub family	0.1	1.30E-01	742	748		
	PC052095U	U	641958		Tropomyosin	Tropomyosin	3.2	1.80E-01	1863	1898		
	PC052095U	U	641958		Lipoprotein_1	Borrelia lipoprotein	2.7	1.80E-01	1781	1809		
	PC052095U	U	641958		HR1	Hr1 repeat motif	-0.6	2.10E-01	1034	1108		
	PC052095U	U	641958		HSP70	Hsp70 protein	-414.1	2.20E-01	600	996		
	PC052095U	U	641958		OEP	Outer membrane efflux protein	-38.3	2.70E-01	1488	1684		
	PC052095U	U	641958		Involucrin	Involucrin repeat	10.5	3.30E-01	1823	1832		
	PC052095U	U	641958		kinesin	Kinesin motor domain	3.1	3.30E-01	1531	1548		
	PC052095U	U	641958		KE2	KE2 family protein	-47.4	4.00E-01	1062	1165		
	PC052095U	U	641958		HlyD	HlyD family secretion protein	-65	5.30E-01	863	1220		
	PC052095U	U	641958		NAP_family	Nucleosome assembly protein (NAP)	2.5	5.40E-01	1107	1127		
	PC052095U	U	641958		UVR	UvrB/uvrC motif	-4.5	6.10E-01	1043	1077		
	PC052095U	U	641958		Birna_VP5	Birnavirus VP5 protein	-36.2	7.30E-01	1232	1353		
	PC052095U	U	641958		BAR	BAR domain	-110.7	7.90E-01	1325	1534		
	PC052095U	U	641958		Transaldolase	Transaldolase	1	8.20E-01	1304	1317		
	PC052095U	U	641958		PV_RdRp	Viral RNA dependent RNA polymerase	0.5	9.60E-01	1182	1210		
PC129	PC060144D	D	4758200	Down-regulated	NM_004415.1 Homo sapiens desmoplakin (DPI, DPII) (DSP) mRNA [redacted]							
	PC060144D	D	4758200		Plectin_repeat	Plectin repeat	537.6	4.50E-159	2724	2768		
	PC060144D	D	4758200		bZIP	bZIP transcription factor	23.9	1.60E-06	1702	1740		
	PC060144D	D	4758200		spectrin	Spectrin repeat	24.2	1.60E-06	1060	1082		
	PC060144D	D	4758200		Myosin_tail	Myosin tail	9.3	7.00E-03	1394	1416		
	PC060144D	D	4758200		M	M protein repeat	16.6	3.10E-02	1876	1896		
	PC060144D	D	4758200		G-gamma	GGL domain	5.8	9.60E-02	1892	1908		
	PC060144D	D	4758200		Exo70	Exo70 exocyst complex subunit	-263.9	1.90E-01	1779	2352		
	PC060144D	D	4758200		HALZ	Homeobox associated leucine zipper	7.4	2.90E-01	1382	1426		
	PC060144D	D	4758200		RNA_pol_B	RNA polymerase beta subunit	0.2	6.90E-01	2401	2413		
	PC060144D	D	4758200		HR1	Hr1 repeat motif	-6.6	7.40E-01	1844	1918		
	PC060144D	D	4758200		DNA_pol_B_exo	DNA polymerase family B, exonuclease	1.5	7.50E-01	2713	2736		
	PC060144D	D	4758200		Troponin	Troponin	-34.7	7.50E-01	1666	1818		

Table 3

	PC060144D	D	4758200		phoslip	Phospholipase A2	3	7.70E-01	2553	2566		
	PC060144D	D	4758200		Transposase_12	Transposase	-162.5	7.80E-01	1412	1720		
	PC060144D	D	4758200		integrase_DNA	DNA binding domain of tn916 integrase	-7.2	8.80E-01	259	328		
	PC060144D	D	4758200		filament	Intermediate filament protein	1.8	9.80E-01	1552	1582		
	PC060144D	D	4758200		Translin	Translin family	-86.4	9.90E-01	1283	1438		
PC132	PC060441U	U	1688258		HSCOLAG Human collagenase and stromelysin genes, complete cds, and metalloelastase gene, partial cds [redacted]							
	PC060441U	U	1688258		Peptidase_M10	Matrixin	415.2	3.10E-122	37	204		
	PC060441U	U	1688258		hemopexin	Hemopexin	222.2	3.80E-64	426	466		
	PC060441U	U	1688258		Astacin	Astacin (Peptidase family M12A)	-101.3	1.60E-02	107	264		
	PC060441U	U	1688258		PG_binding_1	Putative peptidoglycan binding domain	-3.3	2.60E-02	27	91		
	PC060441U	U	1688258		UDPGP	UTP--glucose-1-phosphate uridylyltran	1.9	8.40E-01	248	266		
PC130	PC060443U	U	4506731		Homo sapiens ribosomal protein S6 (RPS6) mRNA [redacted]							
	PC060443U	U	4506731		Ribosomal_S6e	Ribosomal protein S6e	312.2	3.30E-91	1	127		
PC124	PC060474U	U	4759322		Homo sapiens wingless-type MMTV integration site family, member 2B (WNT2B) mRNA [redacted]							
	PC060474U	U	4759322		wnt	wnt family	656.5	1.00E-239	52	361		
	PC060474U	U	4759322		Keratin_B2	Keratin, high sulfur B2 protein	-87.2	8.50E-01	224	364		
PC152	PC060529U	U	4503821		Homo sapiens FYN-binding protein (FYB-120/130) (FYB) mRNA, and translated products [redacted]							
	PC060529U	U	4503821		SH3	SH3 domain	-7	3.10E-02	514	570		
	PC060529U	U	4503821		vATP-synt_E	ATP synthase (E/31 kDa) subunit	-104.2	9.80E-01	464	645		
PC197	PC060743D	D	4557257	Down-regulated	Homo sapiens adenylate cyclase 8 (brain) (ADCY8) mRNA [redacted]							
	PC060743D	D	4557257		guanylate_cyc	Adenylate and Guanylate cyclase catal	632	1.80E-187	973	1172		
	PC060743D	D	4557257		Bac_export_3	Bacterial export proteins, family 3	-39.6	3.80E-01	292	347		
	PC060743D	D	4557257		GARS	Phosphoribosylglycinamide synthetase,	-92.8	5.50E-01	13	320		
	PC060743D	D	4557257		prion	Prion protein	-98.1	7.50E-01	52	268		
	PC060743D	D	4557257		TrkH	Sodium transport protein	-223.6	9.40E-01	42	454		
PC193	PC060793D	D	4507583	Down-regulated	NM_000043.1 Homo sapiens tumor necrosis factor receptor superfamily [redacted]							
	PC060793D	D	4507583		TNFR_c6	TNFR/NGFR cysteine-rich region	94.9	8.30E-26	129	165		
	PC060793D	D	4507583		death	Death domain	70.7	1.60E-18	231	314		
PC199	PC060940U	U	5052075		Homo sapiens PAPS synthetase-2 (PAPSS2) mRNA [redacted]							
	PC060940U	U	5052075		ATP-sulfurylase	ATP-sulfurylase	683.7	4.70E-203	284	612		
	PC060940U	U	5052075		APS_kinase	Adenylylsulfate kinase	395.1	3.60E-116	41	199		
	PC060940U	U	5052075		Thymidylate_kin	Thymidylate kinase	-70	2.30E-01	47	207		
	PC060940U	U	5052075		6PF2K	6-phosphofructo-2-kinase	-123.6	3.20E-01	30	223		
	PC060940U	U	5052075		PRK	Phosphoribulokinase / Uridine kinase	3.1	3.90E-01	47	66		
PC188	PC061342D	D	386831	Down-regulated	HUMINTEO4 Human leukocyte adhesion protein p150,95 alpha subunit gene, exons 16-2 [redacted]							
	PC061342D	D	386831		vwa	von Willebrand factor type A domain	239.3	2.80E-69	151	329		
	PC061342D	D	386831		FG-GAP	FG-GAP repeat	200.6	1.30E-57	581	633		
	PC061342D	D	386831		integrin_A	Integrin alpha cytoplasmic region	30.6	1.90E-06	1129	1143		
	PC061342D	D	386831		Polyoma_coat2	Polyomavirus coat protein	1.3	6.10E-01	522	531		
PC184	PC061477U	U	4506387		Homo sapiens RAD23 (S. cerevisiae) homolog B (RAD23B) mRNA [redacted]							
	PC061477U	U	4506387		ubiquitin	Ubiquitin family	105.2	3.20E-29	1	78		
	PC061477U	U	4506387		UBA	UBA/TS-N domain	71.5	9.40E-19	365	404		
	PC061477U	U	4506387		integrin_B	Integrins, beta chain	6.2	4.10E-03	364	391		
PC213	PC061528D	D	4506701	Down-regulated	Homo sapiens ribosomal protein S23 (RPS23) mRNA [redacted]							

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Table 3

	PC061528D	D	4506701		Ribosomal_S12	Ribosomal protein S12	279.8	1.80E-81	7	142	
PC202	PC061779U	U	4504767		[Homo sapiens]integrin beta-1 (fibronectin receptor beta) polypeptide (antigen CD29 includes MDF2 MSK12) (ITGB1) mRNA						
	PC061779U	U	4504767		integrin_B	Integrins, beta chain	1121.8	0.00E+00	34	464	
	PC061779U	U	4504767		EGF	EGF-like domain	21.3	1.20E-03	599	630	
	PC061779U	U	4504767		Plexin_repeat	Plexin repeat	7.7	2.00E-02	26	76	
	PC061779U	U	4504767		PNTB	NAD(P) transhydrogenase beta subunit	4.1	1.40E-01	2	20	
	PC061779U	U	4504767		metalthio	Metallothionein	-6.8	1.70E-01	594	667	
PC214	PC061827U	U	7382496		[Homo sapiens]p21/Cdc42/Rac1-activated kinase 1 (yeast STE20-related) (PAK1) mRNA						
	PC061827U	U	7382496		pkinase	Protein kinase domain	312.4	2.90E-91	270	521	
	PC061827U	U	7382496		PBD	P21-Rho-binding domain	127	1.80E-35	75	135	
	PC061827U	U	7382496		kinesin	Kinesin motor domain	3.4	2.70E-01	228	250	
	PC061827U	U	7382496		ABC1	ABC1 family	-57.1	1.00E+00	261	386	
PC208	PC061839U	U	8394499		[Homo sapiens]ubiquitin associated protein (UBAP) mRNA						
	PC061839U	U	8394499		UBA	UBA/TS-N domain	23.1	3.50E-04	459	498	
PC147	PC070152U	U	4506713		[Homo sapiens]ribosomal protein S27a (RPS27A) mRNA						
	PC070152U	U	4506713		ubiquitin	Ubiquitin family	153.2	2.40E-43	1	74	
	PC070152U	U	4506713		Ribosomal_S27	Ribosomal protein S27a	121	1.10E-33	101	147	
	PC070152U	U	4506713		IBR	IBR domain	-22.5	9.70E-01	103	156	
PC174	PC070343U	U	4507211		[Homo sapiens]signal recognition particle 14kD (homologous Alu RNA-binding protein) (SRP14) mRNA						
	PC070343U	U	4507211		SRP14	Signal recognition particle 14kD prot	216.4	2.10E-62	4	94	
PC175	PC070436D	D	4503287	Down-regulated	NM_001675 [Homo sapiens]growth arrest and DNA-damage-inducible						
	PC070436D	D	4503287		Ribosomal_L7Ae	Ribosomal protein L7Ae/L30e/S12e/Gad	73.6	2.10E-19	21	123	
PC173	PC070544U	U	7765076		S76438 [ribosomal protein [human, colon, mRNA, 826 nt]						
	PC070544U	U	7765076		Ribosomal_S3_C	Ribosomal protein S3, C-terminal domai	112.8	1.30E-35	104	188	
	PC070544U	U	7765076		KH-domain	KH domain	24.7	1.10E-04	47	95	
PC257	PC070729U	U	8923791		[Homo sapiens]aPS beta protein (HSRTSBETA) mRNA						
	PC070729U	U	8923791		MR_MLE	Mandelate racemase / muconate lactoni	44.5	2.40E-13	191	328	
	PC070729U	U	8923791		MR_MLE_N	Mandelate racemase / muconate lactoni	17	1.50E-05	9	112	
	PC070729U	U	8923791		Peptidase_S26	Signal peptidase I	3.8	1.90E-01	54	84	
PC251	PC071770D	D	31442	Down-regulated	HSENRB [Human mRNA for integrin beta 1 subunit precursor						
	PC071770D	D	31442		integrin_B	Integrins, beta chain	1121.8	0.00E+00	34	464	
	PC071770D	D	31442		EGF	EGF-like domain	21.3	1.20E-03	599	630	
	PC071770D	D	31442		Plexin_repeat	Plexin repeat	7.7	2.00E-02	26	76	
	PC071770D	D	31442		PNTB	NAD(P) transhydrogenase beta subunit	4.1	1.40E-01	2	20	
	PC071770D	D	31442		metalthio	Metallothionein	-6.8	1.70E-01	594	667	
PC253	PC071851U	U	15297004		AF059239 [Homo sapiens clone IB18 unknown mRNA						
	PC071851U	U	15297004								
PC159	PC080139D	D	7657160	Down-regulated	NM_001436 [Homo sapiens]3-hydroxyisobutyryl-Coenzyme A hydrolase (HIBCH) mRNA						
	PC080139D	D	7657160		ECH	Enoyl-CoA hydratase/isomerase family	63.6	2.30E-16	42	213	
	PC080139D	D	7657160		RNase_HII	Ribonuclease HII	-94.9	4.50E-01	205	357	
PC156	PC080348U	U	9623361		AF261688 [Homo sapiens]DNA polymerase epsilon p12 subunit gene, complete cds						
	PC080348U	U	9623361		CBFD_NFYB_HMF	Histone-like transcription factor (CBF/	9.7	4.10E-03	39	106	
	PC080348U	U	9623361		TAF	TATA box binding protein associated fa	-14.3	1.10E-01	55	104	
PC163	PC080435D	D	4758808	Down-regulated	[Homo sapiens]rab GTPase activating protein-like (NGAP) mRNA						

Table 3

	PC080435D	D	4758808		RasGAP	GTPase-activator protein for Ras-like	111.4	8.70E-31	348	520	
	PC080435D	D	4758808		PH	PH domain	19.9	1.90E-05	111	158	
	PC080435D	D	4758808		complex1_49Kd	Respiratory-chain NADH dehydrogenase	8.4	3.90E-04	351	359	
	PC080435D	D	4758808		DEAD	DEAD/DEAH box helicase	8.8	3.70E-03	950	992	
	PC080435D	D	4758808		C2	C2 domain	-5.8	4.60E-02	171	251	
	PC080435D	D	4758808		FliD	Flagellar hook-associated protein 2	-242	3.50E-01	603	1101	
PC216	PC080511U	U	4504191		NM_000179 [Homo sapiens mutS (E coli) homolog 6 (MSH6)						
	PC080511U	U	4504191		MutS_C	DNA mismatch repair proteins, mutS fa	322.1	3.30E-94	1054	1316	
	PC080511U	U	4504191		MutS_N	MutS family, N-terminal putative DNA	216.6	2.00E-62	409	977	
	PC080511U	U	4504191		PWWP	PWWP domain	127.1	1.60E-35	89	162	
	PC080511U	U	4504191		SNF	Sodium:neurotransmitter symporter fam	1.3	7.30E-01	753	768	
	PC080511U	U	4504191		Luteo_ORF3	Luteovirus (ORF3) RNA-directed RNA	-0.3	8.60E-01	1304	1330	
PC274	PC080742U	U	4507187		NM_003125 [Homo sapiens]small proline-rich protein 1B (cornifin)						
	PC080742U	U	4507187		Cornifin	Cornifin (SPRR) family	57	2.10E-14	1	87	
PC299	PC090230U	U	3252911		AF056322 [Homo sapiens]SP100-HMG nuclear autoantigen (SP100) mRNA, complete cds						
	PC090230U	U	3252911		SAND	SAND domain	180	2.10E-51	595	676	
	PC090230U	U	3252911		HMG_box	HMG (high mobility group) box	118.3	7.70E-33	769	837	
PC302	PC090233U	U	4504193		[Homo sapiens]general transcription factor IIB (GTF2B) mRNA						
	PC090233U	U	4504193		transcript_fac2	Transcription factor TFIIB repeat	231.1	8.60E-67	215	285	
	PC090233U	U	4504193		cyclin	Cyclin, N-terminal domain	-26.6	8.30E-02	94	207	
PC316	PC090622D	D	4506859	Down-regulated	NM_002899 [Homo sapiens]syndecan 1 (SDC1) mRNA						
	PC090622D	D	4506859		Syndecan	Syndecan domain	534.3	6.50E-187	3	308	
PC315	PC090625U	U	7706216		[Homo sapiens]47K binding factor 2 (LOC51510) mRNA						
	PC090625U	U	7706216		TIG	IPT/TIG domain	55.5	6.20E-14	275	365	
	PC090625U	U	7706216		ig	Immunoglobulin domain	11.7	2.40E-03	165	221	
PC310	PC090677D	D	307218	Down-regulated	HUMMHB Al23 [Human MHG protein homologous to chicken B complex protein mRNA, complete cds						
	PC090677D	D	307218		WD40	WD domain, G-beta repeat	200.3	1.60E-57	275	311	
PC239	PC090722D	D	7670748	Down-regulated	AF222906 [Homo sapiens UDP-glucose:glycoprotein glucosyltransferase 2 precursor mRNA, complete cds						
PC230	PC090754U	U	4503473		[Homo sapiens]eukaryotic translation elongation factor 1 alpha 1 (EEF1A1) mRNA						
	PC090754U	U	4503473		GTP_EFTU	Elongation factor Tu GTP binding domai	237.8	8.20E-69	4	175	
	PC090754U	U	4503473		GTP_EFTU_D3	Elongation factor Tu C-terminal domai	201.1	8.80E-58	269	378	
	PC090754U	U	4503473		GTP_EFTU_D2	Elongation factor Tu domain 2	98.6	1.50E-27	187	263	
PC220	PC090788D	D	5031639	Down-regulated	[Homo sapiens]conichon-like (GNIL) mRNA						
	PC090788D	D	5031639								
PC233	PC090842U	U	4557032		[Homo sapiens]lactate dehydrogenase B (LDHB) mRNA						
	PC090842U	U	4557032		ldh_C	lactate/malate dehydrogenase, alpha/beta	297	1.20E-86	164	333	
	PC090842U	U	4557032		ldh	lactate/malate dehydrogenase, NAD bind	284.4	7.30E-83	19	162	
PC236	PC091028U	U	7662426		[Homo sapiens]KIAA0976 protein (KIAA0976) mRNA						
	PC091028U	U	7662426		laminin_Nterm	Laminin N-terminal (Domain VI)	37	8.80E-14	50	295	
	PC091028U	U	7662426		laminin_EGF	Laminin EGF-like (Domains III and V)	31.8	8.00E-07	297	341	
	PC091028U	U	7662426		EGF	EGF-like domain	3.9	5.20E-01	299	326	
PC324	PC091425U	U	4732026		AF183869 [Homo sapiens angiotensin I converting enzyme precursor						
	PC091425U	U	4732026		Peptidase_M2	Angiotensin-converting enzyme	3415	0.00E+00	634	1228	
	PC091425U	U	4732026		HupF_HypC	HupF/HypC family	-34	5.00E-01	1231	1286	

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Table 3

	PC091425U	U	4732026		Phosphoprotein	Vesiculovirus phosphoprotein	0.1	7.10E-01	596	607		
	PC091425U	U	4732026		MM_CoA_mutase	Methylmalonyl-CoA mutase	0.9	7.70E-01	192	221		
PC400	PC091527U	U	5803092		[illegible]							
	PC091527U	U	5803092		Peptidase_M24	metallopeptidase family M24	319	2.80E-93	159	404		
	PC091527U	U	5803092		PBP_GOBP	PBP/GOBP family	-51.4	9.10E-01	127	254		
PC407	PC091839U	U	7158647		[illegible]							
PC405	PC091853U	U	31092		[illegible]							
	PC091853U	U	31092		GTP_EFTU	Elongation factor Tu GTP binding doma	378.7	3.00E-111	5	239		
	PC091853U	U	31092		GTP_EFTU_D3	Elongation factor Tu C-terminal domai	212.7	3.00E-61	333	442		
	PC091853U	U	31092		GTP_EFTU_D2	Elongation factor Tu domain 2	100.7	3.80E-28	251	327		
	PC091853U	U	31092		pyr_redox	Pyridine nucleotide-disulphide oxidor	-99.3	6.10E-01	9	286		
	PC091853U	U	31092		ATP-bind	Conserved hypothetical ATP binding pr	-138.3	9.80E-01	9	182		
PC402	PC091888U	U	4757810		[illegible]							
	PC091888U	U	4757810		ATP-synt_ab	ATP synthase alpha/beta family, nucleo	554.9	2.80E-164	138	421		
	PC091888U	U	4757810		ATP-synt_ab_C	ATP synthase alpha/beta chain, C termi	140.6	1.40E-39	423	531		
	PC091888U	U	4757810		ATP-synt_ab_N	ATP synthase alpha/beta family, beta-b	76.5	2.80E-20	67	135		
	PC091888U	U	4757810		FwdE	Tungsten formylmethanofuran dehydroc	-97.9	9.90E-01	230	408		
PC401	PC092004U	U	8922824		[illegible]							
	PC092004U	U	8922824		zf-C2H2	Zinc finger, C2H2 type	455.9	1.80E-134	457	479		
	PC092004U	U	8922824		zf-BED	BED zinc finger	4.8	2.00E-02	246	284		
	PC092004U	U	8922824		LIM	LIM domain	-16.7	2.30E-01	431	483		
	PC092004U	U	8922824		BolA	BolA-like protein	-24.5	2.70E-01	100	157		
	PC092004U	U	8922824		zf-MIZ	MIZ zinc finger	-21.1	4.70E-01	354	412		
	PC092004U	U	8922824		TFIIS	Transcription factor S-II (TFIIS)	-6.9	4.90E-01	289	327		
	PC092004U	U	8922824		PHD	PHD-finger	-20.8	7.90E-01	122	185		
	PC092004U	U	8922824		zf-ANI	ANI-like Zinc finger	-11.8	8.20E-01	123	169		
PC406	PC092052U	U	4505635		[illegible]							
	PC092052U	U	4505635		cadherin	Cadherin domain	399.8	1.40E-117	749	840		
	PC092052U	U	4505635		Adeno_E3_CR2	Adenovirus E3 region protein CR2	-2.9	2.90E-01	873	912		
	PC092052U	U	4505635		Herpes_gE	Alphaherpesvirus glycoprotein E	-257.7	3.90E-01	552	948		
	PC092052U	U	4505635		CBD_6	Cellulose binding domain	-23.5	6.10E-01	627	786		
PC279	PC100113U	U	5733684		[illegible]							
	PC100113U	U	5733684		trypsin	Trypsin	277	1.90E-88	30	245		
	PC100113U	U	5733684		toxin_4	Anenome neurotoxin	-3.3	4.70E-01	200	239		
PC285	PC100356U	U	13272790		[illegible]							
	PC100356U	U	13272790		oxidored_q1	NADH-Ubiquinone/plastoquinone (com	344.3	6.80E-101	112	404		
	PC100356U	U	13272790		oxidored_q5_N	NADH-ubiquinone oxidoreductase chain	211.7	5.80E-61	1	109		
	PC100356U	U	13272790		sugar_tr	Sugar (and other) transporter	-201.8	6.50E-01	32	411		
	PC100356U	U	13272790		DsbD	Cytochrome C biogenesis protein trans	-101.5	7.50E-01	126	305		
	PC100356U	U	13272790		DUF6	Integral membrane protein DUF6	-29.6	9.80E-01	286	408		
PC294	PC100428U	U	4502981		[illegible]							
	PC100428U	U	4502981		COX4	Cytochrome c oxidase subunit IV	242.1	4.00E-70	26	169		
PC323	PC101430U	U	182851		[illegible]							
	PC101430U	U	182851									

Table 3

PC314	PC101847D	D	5902022	Down-regulated	[illegible]							
	PC101847D	D	5902022		OMPdecase	Orotidine 5'-phosphate decarboxylase	6.7	2.40E-02	274	298		
	PC101847D	D	5902022		Polysacc_synt	Polysaccharide biosynthesis protein	-96.8	8.60E-01	10	289		
PC312	PC101863U	U	35038		[illegible]							
	PC101863U	U	35038		ku	KU domain	570	7.70E-169	1	467		
	PC101863U	U	35038		filament	Intermediate filament protein	2.8	5.40E-01	559	568		
PC417	PC110249D	D	4759258	Down-regulated	[illegible]							
	PC110249D	D	4759258		zf-BED	BED zinc finger	75.8	4.80E-20	23	72		
PC429	PC110541D	D	5031779	Down-regulated	[illegible]							
	PC110541D	D	5031779		HIN	HIN-200/IFI120x domain	887.5	2.00E-264	518	685		
	PC110541D	D	5031779		PAAD_DAPIN	PAAD/DAPIN/Pyrin domain	155.2	5.90E-44	3	88		
	PC110541D	D	5031779		lipocalin	Lipocalin / cytosolic fatty-acid bind	8.8	1.20E-02	639	685		
	PC110541D	D	5031779		pp-binding	Phosphopantetheine attachment site	3.9	1.00E+00	67	82		
PC440	PC110927U	U	7020307		[illegible]							
	PC110927U	U	7020307		oxidored_q1	NADH-Ubiquinone/plastoquinone (com	21.6	2.20E-06	674	712		
PC439	PC110940D	D	4758950	Down-regulated	[illegible]							
	PC110940D	D	4758950		pro_isomerase	Cyclophilin type peptidyl-prolyl cis-tr	395.4	3.00E-116	45	206		
PC443	PC111168U	U	4759284		[illegible]							
	PC111168U	U	4759284		UCH	Ubiquitin carboxyl-terminal hydrolase	465	3.20E-137	1	201		
PC441	PC111181U	U	7416941		[illegible]							
	PC111181U	U	7416941		Tim17	Mitochondrial import inner membrane t	-59.6	6.10E-02	59	210		
	PC111181U	U	7416941		Synapsin	Synapsin, N-terminal domain	4	1.90E-01	86	96		
PC448	PC111588D	D	4503413	Down-regulated	[illegible]							
	PC111588D	D	4503413		EGF	EGF-like domain	31	1.40E-06	108	143		
PC462	PC111669D	D	7705823	Down-regulated	[illegible]							
	PC111669D	D	7705823		Acetyltransf	Acetyltransferase (GNAT) family	70.4	1.90E-18	45	129		
PC458	PC120136U	U	7706729		[illegible]							
	PC120136U	U	7706729		T-box	T-box	380.6	8.10E-112	240	306		
PC460	PC120331U	U	4504425		[illegible]							
	PC120331U	U	4504425		HMG_box	HMG (high mobility group) box	197	1.50E-56	95	163		
PC494	PC120740D	D	36796	Down-regulated	[illegible]							
	PC120740D	D	36796		cpn60_TCP1	TCP-1/cpn60 chaperonin family	808	1.80E-240	28	535		
	PC120740D	D	36796		ATP-synt_B	ATP synthase B/B' CF(0)	4	3.60E-01	302	337		
PC493	PC120741D	D	5174389	Down-regulated	[illegible]							
	PC120741D	D	5174389		thiolase	Thiolase, N-terminal domain	419.2	1.90E-123	1	268		
	PC120741D	D	5174389		thiolase_C	Thiolase, C-terminal domain	250.2	1.50E-72	272	396		
	PC120741D	D	5174389		ketoacyl-synt	Beta-ketoacyl synthase, N-terminal do	-118	3.40E-01	5	154		
PC485	PC121671U	U	7661636		[illegible]							
	PC121671U	U	7661636									

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<213> Homo sapiens

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His Thr Tyr Arg Gln His Ile Val Asn Asp Met Asn Pro Gly Asn Leu
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        355                 360                 365

Gly Ala His Leu Asp Ile Thr Pro Asn Ser Gly Ala Ala Gly Asn Ser
    370                 375                 380

Ala Gly Pro Lys Ser Met Glu Val Ser Cys
385                 390
```

<210> 109
<211> 780
<212> PRT
<213> Homo sapiens

<400> 109

```
Met Thr His Glu Glu His His Ala Ala Lys Thr Leu Gly Ile Gly Lys
1               5                   10                  15

Ala Ile Ala Val Leu Thr Ser Gly Gly Asp Ala Gln Gly Met Asn Ala
            20                  25                  30

Ala Val Arg Ala Val Val Arg Val Gly Ile Phe Thr Gly Ala Arg Val
        35                  40                  45

Phe Phe Val His Glu Gly Tyr Gln Gly Leu Val Asp Gly Gly Asp His
    50                  55                  60

Ile Lys Glu Ala Thr Trp Glu Ser Val Ser Met Met Leu Gln Leu Gly
65                  70                  75                  80

Gly Thr Val Ile Gly Ser Ala Arg Cys Lys Asp Phe Arg Glu Arg Glu
                85                  90                  95

Gly Arg Leu Arg Ala Ala Tyr Asn Leu Val Lys Arg Gly Ile Thr Asn
            100                 105                 110

Leu Cys Val Ile Gly Gly Asp Gly Ser Leu Thr Gly Ala Asp Thr Phe
        115                 120                 125

Arg Ser Glu Trp Ser Asp Leu Leu Ser Asp Leu Gln Lys Ala Gly Lys
    130                 135                 140

Ile Thr Asp Glu Glu Ala Thr Lys Ser Ser Tyr Leu Asn Ile Val Gly
145                 150                 155                 160

Leu Val Gly Ser Ile Asp Asn Asp Phe Cys Gly Thr Asp Met Thr Ile
                165                 170                 175
```



```
Gly Thr Asp Ser Ala Leu His Arg Ile Met Glu Ile Val Asp Ala Ile
            180                 185                 190

Thr Thr Thr Ala Gln Ser His Gln Arg Thr Phe Val Leu Glu Val Met
        195                 200                 205

Gly Arg His Cys Gly Tyr Leu Ala Leu Val Thr Ser Leu Ser Cys Gly
    210                 215                 220

Ala Asp Trp Val Phe Ile Pro Glu Cys Pro Pro Asp Asp Asp Trp Glu
225                 230                 235                 240

Glu His Leu Cys Arg Arg Leu Ser Glu Thr Arg Thr Arg Gly Ser Arg
                245                 250                 255

Leu Asn Ile Ile Ile Val Ala Glu Gly Ala Ile Asp Lys Asn Gly Lys
            260                 265                 270

Pro Ile Thr Ser Glu Asp Ile Lys Asn Leu Val Val Lys Arg Leu Gly
        275                 280                 285

Tyr Asp Thr Arg Val Thr Val Leu Gly His Val Gln Arg Gly Gly Thr
    290                 295                 300

Pro Ser Ala Phe Asp Arg Ile Leu Gly Ser Arg Met Gly Val Glu Ala
305                 310                 315                 320

Val Met Ala Leu Leu Glu Gly Thr Pro Asp Thr Pro Ala Cys Val Val
                325                 330                 335

Ser Leu Ser Gly Asn Gln Ala Val Arg Leu Pro Leu Met Glu Cys Val
            340                 345                 350

Gln Val Thr Lys Asp Val Thr Lys Ala Met Asp Glu Lys Lys Phe Asp
        355                 360                 365

Glu Ala Leu Lys Leu Arg Gly Arg Ser Phe Met Asn Asn Trp Glu Val
    370                 375                 380

Tyr Lys Leu Leu Ala His Val Arg Pro Pro Val Ser Lys Ser Gly Ser
385                 390                 395                 400

His Thr Val Ala Val Met Asn Val Gly Ala Pro Ala Ala Gly Met Asn
                405                 410                 415

Ala Ala Val Arg Ser Thr Val Arg Ile Gly Leu Ile Gln Gly Asn Arg
            420                 425                 430

Val Leu Val Val His Asp Gly Phe Glu Gly Leu Ala Lys Gly Gln Ile
        435                 440                 445

Glu Glu Ala Gly Trp Ser Tyr Val Gly Gly Trp Thr Gly Gln Gly Gly
    450                 455                 460

Ser Lys Leu Gly Thr Lys Arg Thr Leu Pro Lys Lys Ser Phe Glu Gln
465                 470                 475                 480

Ile Ser Ala Asn Ile Thr Lys Phe Asn Ile Gln Gly Leu Val Ile Ile
```

485 490 495

Gly Gly Phe Glu Ala Tyr Thr Gly Gly Leu Glu Leu Met Glu Gly Arg
500 505 510

Lys Gln Phe Asp Glu Leu Cys Ile Pro Phe Val Val Ile Pro Ala Thr
515 520 525

Val Ser Asn Asn Val Pro Gly Ser Asp Phe Ser Val Gly Ala Asp Thr
530 535 540

Ala Leu Asn Thr Ile Cys Thr Thr Cys Asp Arg Ile Lys Gln Ser Ala
545 550 555 560

Ala Gly Thr Lys Arg Arg Val Phe Ile Ile Glu Thr Met Gly Gly Tyr
565 570 575

Cys Gly Tyr Leu Ala Thr Met Ala Gly Leu Ala Ala Gly Ala Asp Ala
580 585 590

Ala Tyr Ile Phe Glu Glu Pro Phe Thr Ile Arg Asp Leu Gln Ala Asn
595 600 605

Val Glu His Leu Val Gln Lys Met Lys Thr Thr Val Lys Arg Gly Leu
610 615 620

Val Leu Arg Asn Glu Lys Cys Asn Glu Asn Tyr Thr Thr Asp Phe Ile
625 630 635 640

Phe Asn Leu Tyr Ser Glu Glu Gly Lys Gly Ile Phe Asp Ser Arg Lys
645 650 655

Asn Val Leu Gly His Met Gln Gln Gly Gly Ser Pro Thr Pro Phe Asp
660 665 670

Arg Asn Phe Ala Thr Lys Met Gly Ala Lys Ala Met Asn Trp Met Ser
675 680 685

Gly Lys Ile Lys Glu Ser Tyr Arg Asn Gly Arg Ile Phe Ala Asn Thr
690 695 700

Pro Asp Ser Gly Cys Val Leu Gly Met Arg Lys Arg Ala Leu Val Phe
705 710 715 720

Gln Pro Val Ala Glu Leu Lys Asp Gln Thr Asp Phe Glu His Arg Ile
725 730 735

Pro Lys Glu Gln Trp Trp Leu Lys Leu Arg Pro Ile Leu Lys Ile Leu
740 745 750

Ala Lys Tyr Glu Ile Asp Leu Asp Thr Ser Asp His Ala His Leu Glu
755 760 765

His Ile Thr Arg Lys Arg Ser Gly Glu Ala Ala Val
770 775 780

<210> 110
<211> 1403
<212> PRT
<213> Homo sapiens

<400> 110

Met Ala Thr Gln Gln Lys Ala Ser Asp Glu Arg Ile Ser Gln Phe Asp
1 5 10 15

His Asn Leu Leu Pro Glu Leu Ser Ala Leu Leu Gly Leu Asp Ala Val
20 25 30

Gln Leu Ala Lys Glu Leu Glu Glu Glu Glu Gln Lys Glu Arg Ala Lys
35 40 45

Met Gln Lys Gly Tyr Asn Ser Gln Met Arg Ser Glu Ala Lys Arg Leu
50 55 60

Lys Thr Phe Val Thr Tyr Glu Pro Tyr Ser Ser Trp Ile Pro Gln Glu
65 70 75 80

Met Ala Ala Ala Gly Phe Tyr Phe Thr Gly Val Lys Ser Gly Ile Gln
85 90 95

Cys Phe Cys Cys Ser Leu Ile Leu Phe Gly Ala Gly Leu Thr Arg Leu
100 105 110

Pro Ile Glu Asp His Lys Arg Phe His Pro Asp Cys Gly Phe Leu Leu
115 120 125

Asn Lys Asp Val Gly Asn Ile Ala Lys Tyr Asp Ile Arg Val Lys Asn
130 135 140

Leu Lys Ser Arg Leu Arg Gly Gly Lys Met Arg Tyr Gln Glu Glu Glu
145 150 155 160

Ala Arg Leu Ala Ser Phe Arg Asn Trp Pro Phe Tyr Val Gln Gly Ile
165 170 175

Ser Pro Cys Val Leu Ser Glu Ala Gly Phe Val Phe Thr Gly Lys Gln
180 185 190

Asp Thr Val Gln Cys Phe Ser Cys Gly Gly Cys Leu Gly Asn Trp Glu
195 200 205

Glu Gly Asp Asp Pro Trp Lys Glu His Ala Lys Trp Phe Pro Lys Cys
210 215 220

Glu Phe Leu Arg Ser Lys Lys Ser Ser Glu Glu Ile Thr Gln Tyr Ile
225 230 235 240

Gln Ser Tyr Lys Gly Phe Val Asp Ile Thr Gly Glu His Phe Val Asn
245 250 255

Ser Trp Val Gln Arg Glu Leu Pro Met Ala Ser Ala Tyr Cys Asn Asp
260 265 270

Ser Ile Phe Ala Tyr Glu Glu Leu Arg Leu Asp Ser Phe Lys Asp Trp
275 280 285

Pro Arg Glu Ser Ala Val Gly Val Ala Ala Leu Ala Lys Ala Gly Leu
290 295 300

Phe Tyr Thr Gly Ile Lys Asp Ile Val Gln Cys Phe Ser Cys Gly Gly
305 310 315 320

Cys Leu Glu Lys Trp Gln Glu Gly Asp Asp Pro Leu Asp Asp His Thr
325 330 335

Arg Cys Phe Pro Asn Cys Pro Phe Leu Gln Asn Met Lys Ser Ser Ala
340 345 350

Glu Val Thr Pro Asp Leu Gln Ser Arg Gly Glu Leu Cys Glu Leu Leu
355 360 365

Glu Thr Thr Ser Glu Ser Asn Leu Glu Asp Ser Ile Ala Val Gly Pro
370 375 380

Ile Val Pro Glu Met Ala Gln Gly Glu Ala Gln Trp Phe Gln Glu Ala
385 390 395 400

Lys Asn Leu Asn Glu Gln Leu Arg Ala Ala Tyr Thr Ser Ala Ser Phe
405 410 415

Arg His Met Ser Leu Leu Asp Ile Ser Ser Asp Leu Ala Thr Asp His
420 425 430

Leu Leu Gly Cys Asp Leu Ser Ile Ala Ser Lys His Ile Ser Lys Pro
435 440 445

Val Gln Glu Pro Leu Val Leu Pro Glu Val Phe Gly Asn Leu Asn Ser
450 455 460

Val Met Cys Val Glu Gly Glu Ala Gly Ser Gly Lys Thr Val Leu Leu
465 470 475 480

Lys Lys Ile Ala Phe Leu Trp Ala Ser Gly Cys Cys Pro Leu Leu Asn
485 490 495

Arg Phe Gln Leu Val Phe Tyr Leu Ser Leu Ser Ser Thr Arg Pro Asp
500 505 510

Glu Gly Leu Ala Ser Ile Ile Cys Asp Gln Leu Leu Glu Lys Glu Gly
515 520 525

Ser Val Thr Glu Met Cys Met Arg Asn Ile Ile Gln Gln Leu Lys Asn
530 535 540

Gln Val Leu Phe Leu Leu Asp Asp Tyr Lys Glu Ile Cys Ser Ile Pro
545 550 555 560

Gln Val Ile Gly Lys Leu Ile Gln Lys Asn His Leu Ser Arg Thr Cys
565 570 575

Leu Leu Ile Ala Val Arg Thr Asn Arg Ala Arg Asp Ile Arg Arg Tyr
580 585 590

Leu Glu Thr Ile Leu Glu Ile Lys Ala Phe Pro Phe Tyr Asn Thr Val
595 600 605

Cys Ile Leu Arg Lys Leu Phe Ser His Asn Met Thr Arg Leu Arg Lys
610 615 620

Phe Met Val Tyr Phe Gly Lys Asn Gln Ser Leu Gln Lys Ile Gln Lys
625 630 635 640

Thr Pro Leu Phe Val Ala Ala Ile Cys Ala His Trp Phe Gln Tyr Pro
645 650 655

Phe Asp Pro Ser Phe Asp Asp Val Ala Val Phe Lys Ser Tyr Met Glu
660 665 670

Arg Leu Ser Leu Arg Asn Lys Ala Thr Ala Glu Ile Leu Lys Ala Thr
675 680 685

Val Ser Ser Cys Gly Glu Leu Ala Leu Lys Gly Phe Phe Ser Cys Cys
690 695 700

Phe Glu Phe Asn Asp Asp Asp Leu Ala Glu Ala Gly Val Asp Glu Asp
705 710 715 720

Glu Asp Leu Thr Met Cys Leu Met Ser Lys Phe Thr Ala Gln Arg Leu
725 730 735

Arg Pro Phe Tyr Arg Phe Leu Ser Pro Ala Phe Gln Glu Phe Leu Ala
740 745 750

Gly Met Arg Leu Ile Glu Leu Leu Asp Ser Asp Arg Gln Glu His Gln
755 760 765

Asp Leu Gly Leu Tyr His Leu Lys Gln Ile Asn Ser Pro Met Met Thr
770 775 780

Val Ser Ala Tyr Asn Asn Phe Leu Asn Tyr Val Ser Ser Leu Pro Ser
785 790 795 800

Thr Lys Ala Gly Pro Lys Ile Val Ser His Leu Leu His Leu Val Asp
805 810 815

Asn Lys Glu Ser Leu Glu Asn Ile Ser Glu Asn Asp Asp Tyr Leu Lys
820 825 830

His Gln Pro Glu Ile Ser Leu Gln Met Gln Leu Leu Arg Gly Leu Trp
835 840 845

Gln Ile Cys Pro Gln Ala Tyr Phe Ser Met Val Ser Glu His Leu Leu
850 855 860

Val Leu Ala Leu Lys Thr Ala Tyr Gln Ser Asn Thr Val Ala Ala Cys
865 870 875 880

Ser Pro Phe Val Leu Gln Phe Leu Gln Gly Arg Thr Leu Thr Leu Gly
885 890 895

Ala Leu Asn Leu Gln Tyr Phe Phe Asp His Pro Glu Ser Leu Ser Leu
900 905 910

Leu Arg Ser Ile His Phe Pro Ile Arg Gly Asn Lys Thr Ser Pro Arg
915 920 925

Ala His Phe Ser Val Leu Glu Thr Cys Phe Asp Lys Ser Gln Val Pro
930 935 940

```
Thr Ile Asp Gln Asp Tyr Ala Ser Ala Phe Glu Pro Met Asn Glu Trp
945                 950                 955                 960

Glu Arg Asn Leu Ala Glu Lys Glu Asp Asn Val Lys Ser Tyr Met Asp
                965                 970                 975

Met Gln Arg Arg Ala Ser Pro Asp Leu Ser Thr Gly Tyr Trp Lys Leu
            980                 985                 990

Ser Pro Lys Gln Tyr Lys Ile Pro  Cys Leu Glu Val Asp  Val Asn Asp
        995                1000                1005

Ile Asp  Val Val Gly Gln Asp  Met Leu Glu Ile Leu  Met Thr Val
    1010                1015                1020

Phe Ser  Ala Ser Gln Arg Ile  Glu Leu His Leu Asn  His Ser Arg
    1025                1030                1035

Gly Phe  Ile Glu Ser Ile Arg  Pro Ala Leu Glu Leu  Ser Lys Ala
    1040                1045                1050

Ser Val  Thr Lys Cys Ser Ile  Ser Lys Leu Glu Leu  Ser Ala Ala
    1055                1060                1065

Glu Gln  Glu Leu Leu Leu Thr  Leu Pro Ser Leu Glu  Ser Leu Glu
    1070                1075                1080

Val Ser  Gly Thr Ile Gln Ser  Gln Asp Gln Ile Phe  Pro Asn Leu
    1085                1090                1095

Asp Lys  Phe Leu Cys Leu Lys  Glu Leu Ser Val Asp  Leu Glu Gly
    1100                1105                1110

Asn Ile  Asn Val Phe Ser Val  Ile Pro Glu Glu Phe  Pro Asn Phe
    1115                1120                1125

His His  Met Glu Lys Leu Leu  Ile Gln Ile Ser Ala  Glu Tyr Asp
    1130                1135                1140

Pro Ser  Lys Leu Val Lys Leu  Ile Gln Asn Ser Pro  Asn Leu His
    1145                1150                1155

Val Phe  His Leu Lys Cys Asn  Phe Phe Ser Asp Phe  Gly Ser Leu
    1160                1165                1170

Met Thr  Met Leu Val Ser Cys  Lys Lys Leu Thr Glu  Ile Lys Phe
    1175                1180                1185

Ser Asp  Ser Phe Phe Gln Ala  Val Pro Phe Val Ala  Ser Leu Pro
    1190                1195                1200

Asn Phe  Ile Ser Leu Lys Ile  Leu Asn Leu Glu Gly  Gln Gln Phe
    1205                1210                1215

Pro Asp  Glu Glu Thr Ser Glu  Lys Phe Ala Tyr Ile  Leu Gly Ser
    1220                1225                1230

Leu Ser  Asn Leu Glu Glu Leu  Ile Leu Pro Thr Gly  Asp Gly Ile
```



```
    1235                1240                1245

Tyr Arg  Val Ala Lys Leu Ile  Ile Gln Gln Cys Gln  Gln Leu His
    1250                1255                1260

Cys Leu  Arg Val Leu Ser Phe  Phe Lys Thr Leu Asn  Asp Asp Ser
    1265                1270                1275

Val Val  Glu Ile Ala Lys Val  Ala Ile Ser Gly Gly  Phe Gln Lys
    1280                1285                1290

Leu Glu  Asn Leu Lys Leu Ser  Ile Asn His Lys Ile  Thr Glu Glu
    1295                1300                1305

Gly Tyr  Arg Asn Phe Phe Gln  Ala Leu Asp Asn Met  Pro Asn Leu
    1310                1315                1320

Gln Glu  Leu Asp Ile Ser Arg  His Phe Thr Glu Cys  Ile Lys Ala
    1325                1330                1335

Gln Ala  Thr Thr Val Lys Ser  Leu Ser Gln Cys Val  Leu Arg Leu
    1340                1345                1350

Pro Arg  Leu Ile Arg Leu Asn  Met Leu Ser Trp Leu  Leu Asp Ala
    1355                1360                1365

Asp Asp  Ile Ala Leu Leu Asn  Val Met Lys Glu Arg  His Pro Gln
    1370                1375                1380

Ser Lys  Tyr Leu Thr Ile Leu  Gln Lys Trp Ile Leu  Pro Phe Ser
    1385                1390                1395

Pro Ile  Ile Gln Lys
    1400
```

<210> 111
<211> 1005
<212> PRT
<213> Homo sapiens

<400> 111

```
Met Met Ser Asp Ala Ser Asp Met Leu Ala Ala Ala Leu Glu Gln Met
1               5                  10                  15

Asp Gly Ile Ile Ala Gly Ser Lys Ala Leu Glu Tyr Ser Asn Gly Ile
            20                  25                  30

Phe Asp Cys Gln Ser Pro Thr Ser Pro Phe Met Gly Ser Leu Arg Ala
        35                  40                  45

Leu His Leu Val Glu Asp Leu Arg Gly Leu Leu Glu Met Met Glu Thr
    50                  55                  60

Asp Glu Lys Glu Gly Leu Arg Cys Gln Ile Pro Asp Ser Thr Ala Glu
65                  70                  75                  80

Thr Leu Val Glu Trp Leu Gln Ser Gln Met Thr Asn Gly His Leu Pro
                85                  90                  95

Gly Asn Gly Asp Val Tyr Gln Glu Arg Leu Ala Arg Leu Glu Asn Asp
```

```
          100                 105                 110

Lys Glu Ser Leu Val Leu Gln Val Ser Val Leu Thr Asp Gln Val Glu
        115                 120                 125

Ala Gln Gly Glu Lys Ile Arg Asp Leu Glu Phe Cys Leu Glu Glu His
    130                 135                 140

Arg Glu Lys Leu Asn Ala Thr Glu Glu Met Leu Gln Gln Glu Leu Leu
145                 150                 155                 160

Ser Arg Thr Ser Leu Glu Thr Gln Lys Leu Asp Leu Met Ala Glu Ile
                165                 170                 175

Ser Asn Leu Lys Leu Lys Leu Thr Ala Val Glu Lys Asp Arg Leu Asp
            180                 185                 190

Tyr Glu Asp Lys Phe Arg Asp Thr Glu Gly Leu Ile Gln Glu Ile Asn
        195                 200                 205

Asp Leu Arg Leu Lys Val Ser Glu Met Asp Ser Glu Arg Leu Gln Tyr
    210                 215                 220

Glu Lys Lys Leu Lys Ser Thr Lys Asp Glu Leu Ala Ser Leu Lys Glu
225                 230                 235                 240

Gln Leu Glu Glu Lys Glu Ser Glu Val Lys Arg Leu Gln Glu Lys Leu
                245                 250                 255

Val Cys Lys Met Lys Gly Glu Gly Val Glu Ile Val Asp Arg Asp Glu
            260                 265                 270

Asn Phe Lys Lys Lys Leu Lys Glu Lys Asn Ile Glu Val Gln Lys Met
        275                 280                 285

Lys Lys Ala Val Glu Ser Leu Met Ala Ala Asn Glu Glu Lys Asp Arg
    290                 295                 300

Lys Ile Glu Asp Leu Arg Gln Cys Leu Asn Arg Tyr Lys Lys Met Gln
305                 310                 315                 320

Asp Thr Val Val Leu Ala Gln Gly Lys Lys Gly Lys Asp Gly Glu Tyr
                325                 330                 335

Glu Glu Leu Leu Asn Ser Ser Ser Ile Ser Ser Leu Leu Asp Ala Gln
            340                 345                 350

Gly Phe Ser Asp Leu Glu Lys Ser Pro Ser Pro Thr Pro Val Met Gly
        355                 360                 365

Ser Pro Ser Cys Asp Pro Phe Asn Thr Ser Val Pro Glu Glu Phe His
    370                 375                 380

Thr Thr Ile Leu Gln Val Ser Ile Pro Ser Leu Leu Pro Ala Thr Val
385                 390                 395                 400

Ser Met Glu Thr Ser Glu Lys Ser Lys Leu Thr Pro Lys Pro Glu Thr
                405                 410                 415
```



```
Ser Phe Glu Glu Asn Asp Gly Asn Ile Ile Leu Gly Ala Thr Val Asp
            420                 425                 430

Thr Gln Leu Arg Asp Lys Leu Leu Thr Ser Ser Leu Gln Lys Ser Ser
        435                 440                 445

Ser Leu Gly Asn Leu Lys Lys Glu Thr Ser Asp Gly Glu Lys Glu Thr
    450                 455                 460

Ile Gln Lys Thr Ser Glu Asp Arg Ala Pro Ala Glu Ser Arg Pro Phe
465                 470                 475                 480

Gly Thr Leu Pro Pro Arg Pro Pro Gly Gln Asp Thr Ser Met Asp Asp
                485                 490                 495

Asn Pro Phe Gly Thr Arg Lys Val Arg Ser Ser Phe Gly Arg Gly Phe
            500                 505                 510

Phe Lys Ile Lys Ser Asn Lys Arg Thr Ala Ser Ala Pro Asn Leu Asp
        515                 520                 525

Arg Lys Arg Ser Ala Ser Ala Pro Thr Leu Ala Glu Thr Glu Lys Glu
    530                 535                 540

Thr Ala Ala His Leu Asp Leu Ala Gly Ala Ser Ser Arg Pro Lys Asp
545                 550                 555                 560

Ser Gln Arg Asn Ser Pro Phe Gln Ile Pro Pro Pro Ser Pro Asp Ser
                565                 570                 575

Lys Lys Lys Ser Arg Gly Ile Met Lys Leu Phe Gly Lys Leu Arg Arg
            580                 585                 590

Ser Gln Ser Thr Thr Phe Asn Pro Asp Asp Met Ser Glu Pro Glu Phe
        595                 600                 605

Lys Arg Gly Gly Thr Arg Ala Thr Ala Gly Pro Arg Leu Gly Trp Ser
    610                 615                 620

Arg Asp Leu Gly Gln Ser Asn Ser Asp Leu Asp Met Pro Phe Ala Lys
625                 630                 635                 640

Trp Thr Lys Glu Gln Val Cys Asn Trp Leu Met Glu Gln Gly Leu Gly
                645                 650                 655

Ser Tyr Leu Asn Ser Gly Lys His Trp Ile Ala Ser Gly Gln Thr Leu
            660                 665                 670

Leu Gln Ala Ser Gln Gln Asp Leu Glu Lys Glu Leu Gly Ile Lys His
        675                 680                 685

Ser Leu His Arg Lys Lys Leu Gln Leu Ala Leu Gln Ala Leu Gly Ser
    690                 695                 700

Glu Glu Glu Thr Asn His Gly Lys Leu Asp Phe Asn Trp Val Thr Arg
705                 710                 715                 720

Trp Leu Asp Asp Ile Gly Leu Pro Gln Tyr Lys Thr Gln Phe Asp Glu
                725                 730                 735
```

```
Gly Arg Val Asp Gly Arg Met Leu His Tyr Met Thr Val Asp Asp Leu
            740                 745                 750

Leu Ser Leu Lys Val Val Ser Val Leu His His Leu Ser Ile Lys Arg
        755                 760                 765

Ala Ile Gln Val Leu Arg Ile Asn Asn Phe Glu Pro Asn Cys Leu Arg
    770                 775                 780

Arg Arg Pro Ser Asp Glu Asn Thr Ile Ala Pro Ser Glu Val Gln Lys
785                 790                 795                 800

Trp Thr Asn His Arg Val Met Glu Trp Leu Arg Ser Val Asp Leu Ala
                805                 810                 815

Glu Tyr Ala Pro Asn Leu Arg Gly Ser Gly Val His Gly Gly Leu Met
            820                 825                 830

Val Leu Glu Pro Arg Phe Asn Val Glu Thr Met Ala Gln Leu Leu Asn
        835                 840                 845

Ile Pro Pro Asn Lys Thr Leu Leu Arg Arg His Leu Ala Thr His Phe
    850                 855                 860

Asn Leu Leu Ile Gly Ala Glu Ala Gln His Gln Lys Arg Asp Ala Met
865                 870                 875                 880

Glu Leu Pro Asp Tyr Val Leu Leu Thr Ala Thr Ala Lys Val Lys Pro
                885                 890                 895

Lys Lys Leu Ala Phe Ser Asn Phe Gly Asn Leu Arg Lys Lys Lys Gln
            900                 905                 910

Glu Asp Gly Glu Glu Tyr Val Cys Pro Met Glu Leu Gly Gln Ala Ser
        915                 920                 925

Gly Ser Ala Ser Lys Lys Gly Phe Lys Pro Gly Leu Asp Met Arg Leu
    930                 935                 940

Tyr Glu Glu Asp Asp Leu Asp Arg Leu Glu Gln Met Glu Asp Ser Glu
945                 950                 955                 960

Gly Thr Val Arg Gln Ile Gly Ala Phe Ser Glu Gly Ile Asn Asn Leu
                965                 970                 975

Thr His Met Leu Lys Glu Asp Asp Met Phe Lys Asp Phe Ala Ala Arg
            980                 985                 990

Ser Pro Ser Ala Ser Ile Thr Asp  Glu Asp Ser Asn Val
        995                 1000                1005
```

<210> 112
<211> 2871
<212> PRT
<213> Homo sapiens

<400> 112

```
Met Ser Cys Asn Gly Gly Ser His Pro Arg Ile Asn Thr Leu Gly Arg
1               5                   10                  15
```



```
Met Ile Arg Ala Glu Ser Gly Pro Asp Leu Arg Tyr Glu Val Thr Ser
            20                  25                  30

Gly Gly Gly Gly Thr Ser Arg Met Tyr Tyr Ser Arg Arg Gly Val Ile
        35                  40                  45

Thr Asp Gln Asn Ser Asp Gly Tyr Cys Gln Thr Gly Thr Met Ser Arg
    50                  55                  60

His Gln Asn Gln Asn Thr Ile Gln Glu Leu Leu Gln Asn Cys Ser Asp
65                  70                  75                  80

Cys Leu Met Arg Ala Glu Leu Ile Val Gln Pro Glu Leu Lys Tyr Gly
                85                  90                  95

Asp Gly Ile Gln Leu Thr Arg Ser Arg Glu Leu Asp Glu Cys Phe Ala
            100                 105                 110

Gln Ala Asn Asp Gln Met Glu Ile Leu Asp Ser Leu Ile Arg Glu Met
        115                 120                 125

Arg Gln Met Gly Gln Pro Cys Asp Ala Tyr Gln Lys Arg Leu Leu Gln
    130                 135                 140

Leu Gln Glu Gln Met Arg Ala Leu Tyr Lys Ala Ile Ser Val Pro Arg
145                 150                 155                 160

Val Arg Arg Ala Ser Ser Lys Gly Gly Gly Gly Tyr Thr Cys Gln Ser
                165                 170                 175

Gly Ser Gly Trp Asp Glu Phe Thr Lys His Val Thr Ser Glu Cys Leu
            180                 185                 190

Gly Trp Met Arg Gln Gln Arg Ala Glu Met Asp Met Val Ala Trp Gly
        195                 200                 205

Val Asp Leu Ala Ser Val Glu Gln His Ile Asn Ser His Arg Gly Ile
    210                 215                 220

His Asn Ser Ile Gly Asp Tyr Arg Trp Gln Leu Asp Lys Ile Lys Ala
225                 230                 235                 240

Asp Leu Arg Glu Lys Ser Ala Ile Tyr Gln Leu Glu Glu Glu Tyr Glu
                245                 250                 255

Asn Leu Leu Lys Ala Ser Phe Glu Arg Met Asp His Leu Arg Gln Leu
            260                 265                 270

Gln Asn Ile Ile Gln Ala Thr Ser Arg Glu Ile Met Trp Ile Asn Asp
        275                 280                 285

Cys Glu Glu Glu Glu Leu Leu Tyr Asp Trp Ser Asp Lys Asn Thr Asn
    290                 295                 300

Ile Ala Gln Lys Gln Glu Ala Phe Ser Ile Arg Met Ser Gln Leu Glu
305                 310                 315                 320

Val Lys Glu Lys Glu Leu Asn Lys Leu Lys Gln Glu Ser Asp Gln Leu
                325                 330                 335
```

```
Val Leu Asn Gln His Pro Ala Ser Asp Lys Ile Glu Ala Tyr Met Asp
            340                 345                 350

Thr Leu Gln Thr Gln Trp Ser Trp Ile Leu Gln Ile Thr Lys Cys Ile
        355                 360                 365

Asp Val His Leu Lys Glu Asn Ala Ala Tyr Phe Gln Phe Phe Glu Glu
    370                 375                 380

Ala Gln Ser Thr Glu Ala Tyr Leu Lys Gly Leu Gln Asp Ser Ile Arg
385                 390                 395                 400

Lys Lys Tyr Pro Cys Asp Lys Asn Met Pro Leu Gln His Leu Leu Glu
                405                 410                 415

Gln Ile Lys Glu Leu Glu Lys Glu Arg Glu Lys Ile Leu Glu Tyr Lys
            420                 425                 430

Arg Gln Val Gln Asn Leu Val Asn Lys Ser Lys Lys Ile Val Gln Leu
        435                 440                 445

Lys Pro Arg Asn Pro Asp Tyr Arg Ser Asn Lys Pro Ile Ile Leu Arg
    450                 455                 460

Ala Leu Cys Asp Tyr Lys Gln Asp Gln Lys Ile Val His Lys Gly Asp
465                 470                 475                 480

Glu Cys Ile Leu Lys Asp Asn Asn Glu Arg Ser Lys Trp Tyr Val Thr
                485                 490                 495

Gly Pro Gly Gly Val Asp Met Leu Val Pro Ser Val Gly Leu Ile Ile
            500                 505                 510

Pro Pro Pro Asn Pro Leu Ala Val Asp Leu Ser Cys Lys Ile Glu Gln
        515                 520                 525

Tyr Tyr Glu Ala Ile Leu Ala Leu Trp Asn Gln Leu Tyr Ile Asn Met
    530                 535                 540

Lys Ser Leu Val Ser Trp His Tyr Cys Met Ile Asp Ile Glu Lys Ile
545                 550                 555                 560

Arg Ala Met Thr Ile Ala Lys Leu Lys Thr Met Arg Gln Glu Asp Tyr
                565                 570                 575

Met Lys Thr Ile Ala Asp Leu Glu Leu His Tyr Gln Glu Phe Ile Arg
            580                 585                 590

Asn Ser Gln Gly Ser Glu Met Phe Gly Asp Asp Asp Lys Arg Lys Ile
        595                 600                 605

Gln Ser Gln Phe Thr Asp Ala Gln Lys His Tyr Gln Thr Leu Val Ile
    610                 615                 620

Gln Leu Pro Gly Tyr Pro Gln His Gln Thr Val Thr Thr Thr Glu Ile
625                 630                 635                 640

Thr His His Gly Thr Cys Gln Asp Val Asn His Asn Lys Val Ile Glu
```



```
                645                 650                 655

Thr Asn Arg Glu Asn Asp Lys Gln Glu Thr Trp Met Leu Met Glu Leu
            660                 665                 670

Gln Lys Ile Arg Arg Gln Ile Glu His Cys Glu Gly Arg Met Thr Leu
        675                 680                 685

Lys Asn Leu Pro Leu Ala Asp Gln Gly Ser Ser His His Ile Thr Val
    690                 695                 700

Lys Ile Asn Glu Leu Lys Ser Val Gln Asn Asp Ser Gln Ala Ile Ala
705                 710                 715                 720

Glu Val Leu Asn Gln Leu Lys Asp Met Leu Ala Asn Phe Arg Gly Ser
                725                 730                 735

Glu Lys Tyr Cys Tyr Leu Gln Asn Glu Val Phe Gly Leu Phe Gln Lys
            740                 745                 750

Leu Glu Asn Ile Asn Gly Val Thr Asp Gly Tyr Leu Asn Ser Leu Cys
        755                 760                 765

Thr Val Arg Ala Leu Leu Gln Ala Ile Leu Gln Thr Glu Asp Met Leu
    770                 775                 780

Lys Val Tyr Glu Ala Arg Leu Thr Glu Glu Glu Thr Val Cys Leu Asp
785                 790                 795                 800

Leu Asp Lys Val Glu Ala Tyr Arg Cys Gly Leu Lys Lys Ile Lys Asn
                805                 810                 815

Asp Leu Asn Leu Lys Lys Ser Leu Leu Ala Thr Met Lys Thr Glu Leu
            820                 825                 830

Gln Lys Ala Gln Gln Ile His Ser Gln Thr Ser Gln Gln Tyr Pro Leu
        835                 840                 845

Tyr Asp Leu Asp Leu Gly Lys Phe Gly Glu Lys Val Thr Gln Leu Thr
    850                 855                 860

Asp Arg Trp Gln Arg Ile Asp Lys Gln Ile Asp Phe Arg Leu Trp Asp
865                 870                 875                 880

Leu Glu Lys Gln Ile Lys Gln Leu Arg Asn Tyr Arg Asp Asn Tyr Gln
                885                 890                 895

Ala Phe Cys Lys Trp Leu Tyr Asp Arg Lys Arg Arg Gln Asp Ser Leu
            900                 905                 910

Glu Ser Met Lys Phe Gly Asp Ser Asn Thr Val Met Arg Phe Leu Asn
        915                 920                 925

Glu Gln Lys Asn Leu His Ser Glu Ile Ser Gly Lys Arg Asp Lys Ser
    930                 935                 940

Glu Glu Val Gln Lys Ile Ala Glu Leu Cys Ala Asn Ser Ile Lys Asp
945                 950                 955                 960
```

Tyr Glu Leu Gln Leu Ala Ser Tyr Thr Ser Gly Leu Glu Thr Leu Leu
965 970 975

Asn Ile Pro Ile Lys Arg Thr Met Ile Gln Ser Pro Ser Gly Val Ile
980 985 990

Leu Gln Glu Ala Ala Asp Val His Ala Arg Tyr Ile Glu Leu Leu Thr
995 1000 1005

Arg Ser Gly Asp Tyr Tyr Arg Phe Leu Ser Glu Met Leu Lys Ser
1010 1015 1020

Leu Glu Asp Leu Lys Leu Lys Asn Thr Lys Ile Glu Val Leu Glu
1025 1030 1035

Glu Glu Leu Arg Leu Ala Arg Asp Ala Asn Ser Glu Asn Cys Asn
1040 1045 1050

Lys Asn Lys Phe Leu Asp Gln Asn Leu Gln Lys Tyr Gln Ala Glu
1055 1060 1065

Cys Ser Gln Phe Lys Ala Lys Leu Ala Ser Leu Glu Glu Leu Lys
1070 1075 1080

Arg Gln Ala Glu Leu Asp Gly Lys Ser Ala Lys Gln Asn Leu Asp
1085 1090 1095

Lys Cys Tyr Gly Gln Ile Lys Glu Leu Asn Glu Lys Ile Thr Arg
1100 1105 1110

Leu Thr Tyr Glu Ile Glu Asp Glu Lys Arg Arg Arg Lys Ser Val
1115 1120 1125

Glu Asp Arg Phe Asp Gln Gln Lys Asn Asp Tyr Asp Gln Leu Gln
1130 1135 1140

Lys Ala Arg Gln Cys Glu Lys Glu Asn Leu Gly Trp Gln Lys Leu
1145 1150 1155

Glu Ser Glu Lys Ala Ile Lys Glu Lys Glu Tyr Glu Ile Glu Arg
1160 1165 1170

Leu Arg Val Leu Leu Gln Glu Glu Gly Thr Arg Lys Arg Glu Tyr
1175 1180 1185

Glu Asn Glu Leu Ala Lys Val Arg Asn His Tyr Asn Glu Glu Met
1190 1195 1200

Ser Asn Leu Arg Asn Lys Tyr Glu Thr Glu Ile Asn Ile Thr Lys
1205 1210 1215

Thr Thr Ile Lys Glu Ile Ser Met Gln Lys Glu Asp Asp Ser Lys
1220 1225 1230

Asn Leu Arg Asn Gln Leu Asp Arg Leu Ser Arg Glu Asn Arg Asp
1235 1240 1245

Leu Lys Asp Glu Ile Val Arg Leu Asn Asp Ser Ile Leu Gln Ala
1250 1255 1260

Thr Glu Gln Arg Arg Arg Ala Glu Glu Asn Ala Leu Gln Gln Lys
1265 1270 1275

Ala Cys Gly Ser Glu Ile Met Gln Lys Lys Gln His Leu Glu Ile
1280 1285 1290

Glu Leu Lys Gln Val Met Gln Gln Arg Ser Glu Asp Asn Ala Arg
1295 1300 1305

His Lys Gln Ser Leu Glu Glu Ala Ala Lys Thr Ile Gln Asp Lys
1310 1315 1320

Asn Lys Glu Ile Glu Arg Leu Lys Ala Glu Phe Gln Glu Glu Ala
1325 1330 1335

Lys Arg Arg Trp Glu Tyr Glu Asn Glu Leu Ser Lys Val Arg Asn
1340 1345 1350

Asn Tyr Asp Glu Glu Ile Ile Ser Leu Lys Asn Gln Phe Glu Thr
1355 1360 1365

Glu Ile Asn Ile Thr Lys Thr Thr Ile His Gln Leu Thr Met Gln
1370 1375 1380

Lys Glu Glu Asp Thr Ser Gly Tyr Arg Ala Gln Ile Asp Asn Leu
1385 1390 1395

Thr Arg Glu Asn Arg Ser Leu Ser Glu Glu Ile Lys Arg Leu Lys
1400 1405 1410

Asn Thr Leu Thr Gln Thr Thr Glu Asn Leu Arg Arg Val Glu Glu
1415 1420 1425

Asp Ile Gln Gln Gln Lys Ala Thr Gly Ser Glu Val Ser Gln Arg
1430 1435 1440

Lys Gln Gln Leu Glu Val Glu Leu Arg Gln Val Thr Gln Met Arg
1445 1450 1455

Thr Glu Glu Ser Val Arg Tyr Lys Gln Ser Leu Asp Asp Ala Ala
1460 1465 1470

Lys Thr Ile Gln Asp Lys Asn Lys Glu Ile Glu Arg Leu Lys Gln
1475 1480 1485

Leu Ile Asp Lys Glu Thr Asn Asp Arg Lys Cys Leu Glu Asp Glu
1490 1495 1500

Asn Ala Arg Leu Gln Arg Val Gln Tyr Asp Leu Gln Lys Ala Asn
1505 1510 1515

Ser Ser Ala Thr Glu Thr Ile Asn Lys Leu Lys Val Gln Glu Gln
1520 1525 1530

Glu Leu Thr Arg Leu Arg Ile Asp Tyr Glu Arg Val Ser Gln Glu
1535 1540 1545

Arg Thr Val Lys Asp Gln Asp Ile Thr Arg Phe Gln Asn Ser Leu
1550 1555 1560

Lys Glu Leu Gln Leu Gln Lys Gln Lys Val Glu Glu Glu Leu Asn
1565 1570 1575

Arg Leu Lys Arg Thr Ala Ser Glu Asp Ser Cys Lys Arg Lys Lys
1580 1585 1590

Leu Glu Glu Glu Leu Glu Gly Met Arg Arg Ser Leu Lys Glu Gln
1595 1600 1605

Ala Ile Lys Ile Thr Asn Leu Thr Gln Gln Leu Glu Gln Ala Ser
1610 1615 1620

Ile Val Lys Lys Arg Ser Glu Asp Asp Leu Arg Gln Gln Arg Asp
1625 1630 1635

Val Leu Asp Gly His Leu Arg Glu Lys Gln Arg Thr Gln Glu Glu
1640 1645 1650

Leu Arg Arg Leu Ser Ser Glu Val Glu Ala Leu Arg Arg Gln Leu
1655 1660 1665

Leu Gln Glu Gln Glu Ser Val Lys Gln Ala His Leu Arg Asn Glu
1670 1675 1680

His Phe Gln Lys Ala Ile Glu Asp Lys Ser Arg Ser Leu Asn Glu
1685 1690 1695

Ser Lys Ile Glu Ile Glu Arg Leu Gln Ser Leu Thr Glu Asn Leu
1700 1705 1710

Thr Lys Glu His Leu Met Leu Glu Glu Glu Leu Arg Asn Leu Arg
1715 1720 1725

Leu Glu Tyr Asp Asp Leu Arg Arg Gly Arg Ser Glu Ala Asp Ser
1730 1735 1740

Asp Lys Asn Ala Thr Ile Leu Glu Leu Arg Ser Gln Leu Gln Ile
1745 1750 1755

Ser Asn Asn Arg Thr Leu Glu Leu Gln Gly Leu Ile Asn Asp Leu
1760 1765 1770

Gln Arg Glu Arg Glu Asn Leu Arg Gln Glu Ile Glu Lys Phe Gln
1775 1780 1785

Lys Gln Ala Leu Glu Ala Ser Asn Arg Ile Gln Glu Ser Lys Asn
1790 1795 1800

Gln Cys Thr Gln Val Val Gln Glu Arg Glu Ser Leu Leu Val Lys
1805 1810 1815

Ile Lys Val Leu Glu Gln Asp Lys Ala Arg Leu Gln Arg Leu Glu
1820 1825 1830

Asp Glu Leu Asn Arg Ala Lys Ser Thr Leu Glu Ala Glu Thr Arg
1835 1840 1845

Val Lys Gln Arg Leu Glu Cys Glu Lys Gln Gln Ile Gln Asn Asp

1850 1855 1860

Leu Asn Gln Trp Lys Thr Gln Tyr Ser Arg Lys Glu Glu Ala Ile
1865 1870 1875

Arg Lys Ile Glu Ser Glu Arg Glu Lys Ser Glu Arg Glu Lys Asn
1880 1885 1890

Ser Leu Arg Ser Glu Ile Glu Arg Leu Gln Ala Glu Ile Lys Arg
1895 1900 1905

Ile Glu Glu Arg Cys Arg Arg Lys Leu Glu Asp Ser Thr Arg Glu
1910 1915 1920

Thr Gln Ser Gln Leu Glu Thr Glu Arg Ser Arg Tyr Gln Arg Glu
1925 1930 1935

Ile Asp Lys Leu Arg Gln Arg Pro Tyr Gly Ser His Arg Glu Thr
1940 1945 1950

Gln Thr Glu Cys Glu Trp Thr Val Asp Thr Ser Lys Leu Val Phe
1955 1960 1965

Asp Gly Leu Arg Lys Lys Val Thr Ala Met Gln Leu Tyr Glu Cys
1970 1975 1980

Gln Leu Ile Asp Lys Thr Thr Leu Asp Lys Leu Leu Lys Gly Lys
1985 1990 1995

Lys Ser Val Glu Glu Val Ala Ser Glu Ile Gln Pro Phe Leu Arg
2000 2005 2010

Gly Ala Gly Ser Ile Ala Gly Ala Ser Ala Ser Pro Lys Glu Lys
2015 2020 2025

Tyr Ser Leu Val Glu Ala Lys Arg Lys Lys Leu Ile Ser Pro Glu
2030 2035 2040

Ser Thr Val Met Leu Leu Glu Ala Gln Ala Ala Thr Gly Gly Ile
2045 2050 2055

Ile Asp Pro His Arg Asn Glu Lys Leu Thr Val Asp Ser Ala Ile
2060 2065 2070

Ala Arg Asp Leu Ile Asp Phe Asp Asp Arg Gln Gln Ile Tyr Ala
2075 2080 2085

Ala Glu Lys Ala Ile Thr Gly Phe Asp Asp Pro Phe Ser Gly Lys
2090 2095 2100

Thr Val Ser Val Ser Glu Ala Ile Lys Lys Asn Leu Ile Asp Arg
2105 2110 2115

Glu Thr Gly Met Arg Leu Leu Glu Ala Gln Ile Ala Ser Gly Gly
2120 2125 2130

Val Val Asp Pro Val Asn Ser Val Phe Leu Pro Lys Asp Val Ala
2135 2140 2145

Leu Ala Arg Gly Leu Ile Asp Arg Asp Leu Tyr Arg Ser Leu Asn
2150 2155 2160

Asp Pro Arg Asp Ser Gln Lys Asn Phe Val Asp Pro Val Thr Lys
2165 2170 2175

Lys Lys Val Ser Tyr Val Gln Leu Lys Glu Arg Cys Arg Ile Glu
2180 2185 2190

Pro His Thr Gly Leu Leu Leu Leu Ser Val Gln Lys Arg Ser Met
2195 2200 2205

Ser Phe Gln Gly Ile Arg Gln Pro Val Thr Val Thr Glu Leu Val
2210 2215 2220

Asp Ser Gly Ile Leu Arg Pro Ser Thr Val Asn Glu Leu Glu Ser
2225 2230 2235

Gly Gln Ile Ser Tyr Asp Glu Val Gly Glu Arg Ile Lys Asp Phe
2240 2245 2250

Leu Gln Gly Ser Ser Cys Ile Ala Gly Ile Tyr Asn Glu Thr Thr
2255 2260 2265

Lys Gln Lys Leu Gly Ile Tyr Glu Ala Met Lys Ile Gly Leu Val
2270 2275 2280

Arg Pro Gly Thr Ala Leu Glu Leu Leu Glu Ala Gln Ala Ala Thr
2285 2290 2295

Gly Phe Ile Val Asp Pro Val Ser Asn Leu Arg Leu Pro Val Glu
2300 2305 2310

Glu Ala Tyr Lys Arg Gly Leu Val Gly Ile Glu Phe Lys Glu Lys
2315 2320 2325

Leu Leu Ser Ala Glu Arg Ala Val Thr Gly Tyr Asn Asp Pro Glu
2330 2335 2340

Thr Gly Asn Ile Ile Ser Leu Phe Gln Ala Met Asn Lys Glu Leu
2345 2350 2355

Ile Glu Lys Gly His Gly Ile Arg Leu Leu Glu Ala Gln Ile Ala
2360 2365 2370

Thr Gly Gly Ile Ile Asp Pro Lys Glu Ser His Arg Leu Pro Val
2375 2380 2385

Asp Ile Ala Tyr Lys Arg Gly Tyr Phe Asn Glu Glu Leu Ser Glu
2390 2395 2400

Ile Leu Ser Asp Pro Ser Asp Asp Thr Lys Gly Phe Phe Asp Pro
2405 2410 2415

Asn Thr Glu Glu Asn Leu Thr Tyr Leu Gln Leu Lys Glu Arg Cys
2420 2425 2430

Ile Lys Asp Glu Glu Thr Gly Leu Cys Leu Leu Pro Leu Lys Glu
2435 2440 2445

Lys Lys Lys Gln Val Gln Thr Ser Gln Lys Asn Thr Leu Arg Lys
2450 2455 2460

Arg Arg Val Val Ile Val Asp Pro Glu Thr Asn Lys Glu Met Ser
2465 2470 2475

Val Gln Glu Ala Tyr Lys Lys Gly Leu Ile Asp Tyr Glu Thr Phe
2480 2485 2490

Lys Glu Leu Cys Glu Gln Glu Cys Glu Trp Glu Glu Ile Thr Ile
2495 2500 2505

Thr Gly Ser Asp Gly Ser Thr Arg Val Val Leu Val Asp Arg Lys
2510 2515 2520

Thr Gly Ser Gln Tyr Asp Ile Gln Asp Ala Ile Asp Lys Gly Leu
2525 2530 2535

Val Asp Arg Lys Phe Phe Asp Gln Tyr Arg Ser Gly Ser Leu Ser
2540 2545 2550

Leu Thr Gln Phe Ala Asp Met Ile Ser Leu Lys Asn Gly Val Gly
2555 2560 2565

Thr Ser Ser Ser Met Gly Ser Gly Val Ser Asp Asp Val Phe Ser
2570 2575 2580

Ser Ser Arg His Glu Ser Val Ser Lys Ile Ser Thr Ile Ser Ser
2585 2590 2595

Val Arg Asn Leu Thr Ile Arg Ser Ser Ser Phe Ser Asp Thr Leu
2600 2605 2610

Glu Glu Ser Ser Pro Ile Ala Ala Ile Phe Asp Thr Glu Asn Leu
2615 2620 2625

Glu Lys Ile Ser Ile Thr Glu Gly Ile Glu Arg Gly Ile Val Asp
2630 2635 2640

Ser Ile Thr Gly Gln Arg Leu Leu Glu Ala Gln Ala Cys Thr Gly
2645 2650 2655

Gly Ile Ile His Pro Thr Thr Gly Gln Lys Leu Ser Leu Gln Asp
2660 2665 2670

Ala Val Ser Gln Gly Val Ile Asp Gln Asp Met Ala Thr Ser Val
2675 2680 2685

Lys Pro Ala Gln Lys Ala Phe Ile Gly Phe Glu Gly Val Lys Gly
2690 2695 2700

Lys Lys Lys Met Ser Ala Ala Glu Ala Val Lys Glu Lys Trp Leu
2705 2710 2715

Pro Tyr Glu Ala Gly Gln Arg Phe Leu Glu Phe Gln Tyr Leu Thr
2720 2725 2730

Gly Gly Leu Val Asp Pro Glu Val His Gly Arg Ile Ser Thr Glu
2735 2740 2745

```
Glu Ala  Ile Arg Lys Gly Phe  Ile Asp Gly Arg Ala  Ala Gln Arg
    2750                2755                2760

Leu Gln  Asp Thr Ser Ser Tyr  Ala Lys Ile Leu Thr  Cys Pro Lys
    2765                2770                2775

Thr Lys  Leu Lys Ile Ser Tyr  Lys Asp Ala Ile Asn  Arg Ser Met
    2780                2785                2790

Val Glu  Asp Ile Thr Gly Leu  Arg Leu Leu Glu Ala  Ala Ser Val
    2795                2800                2805

Ser Ser  Lys Gly Leu Pro Ser  Pro Tyr Asn Met Ser  Ser Ala Pro
    2810                2815                2820

Gly Ser  Arg Ser Gly Ser Arg  Ser Gly Ser Arg Ser  Gly Ser Arg
    2825                2830                2835

Ser Gly  Ser Arg Ser Gly Ser  Arg Arg Gly Ser Phe  Asp Ala Thr
    2840                2845                2850

Gly Asn  Ser Ser Tyr Ser Tyr  Ser Tyr Ser Phe Ser  Ser Ser Ser
    2855                2860                2865

Ile Gly  His
    2870
```

<210> 113
<211> 381
<212> PRT
<213> Homo sapiens

<400> 113

```
Met Trp Arg Leu Met Ser Arg Phe Asn Ala Phe Lys Arg Thr Asn Thr
1               5                  10                  15

Ile Leu His His Leu Arg Met Ser Lys His Thr Asp Ala Ala Glu Glu
            20                  25                  30

Val Leu Leu Glu Lys Lys Gly Cys Ala Gly Val Ile Thr Leu Asn Arg
        35                  40                  45

Pro Lys Phe Leu Asn Ala Leu Thr Leu Asn Met Ile Arg Gln Ile Tyr
    50                  55                  60

Pro Gln Leu Lys Lys Trp Glu Gln Asp Pro Glu Thr Phe Val Ile Ile
65                  70                  75                  80

Ile Lys Gly Ala Gly Gly Lys Ala Phe Cys Ala Gly Gly Asp Ile Arg
                85                  90                  95

Val Ile Ser Glu Ala Glu Lys Ala Lys Gln Lys Ile Ala Pro Val Phe
            100                 105                 110

Phe Arg Glu Glu Tyr Met Leu Asn Asn Ala Val Gly Ser Cys Gln Lys
        115                 120                 125

Pro Tyr Val Ala Leu Ile His Gly Ile Thr Met Gly Gly Gly Val Gly
    130                 135                 140
```



```
Leu Ser Val His Gly Gln Phe Arg Val Ala Thr Glu Lys Cys Leu Phe
145                 150                 155                 160

Ala Met Pro Glu Thr Ala Ile Gly Leu Phe Pro Asp Val Gly Gly Gly
                165                 170                 175

Tyr Phe Phe Ala Thr Thr Pro Arg Lys Thr Trp Leu Leu Pro Cys Ile
            180                 185                 190

Asn Gly Phe Arg Leu Lys Gly Arg Asp Val Tyr Arg Ala Gly Ile Ala
        195                 200                 205

Thr His Phe Val Asp Ser Glu Lys Leu Ala Met Leu Glu Glu Asp Leu
    210                 215                 220

Leu Ala Leu Lys Ser Pro Ser Lys Glu Asn Ile Ala Ser Val Leu Glu
225                 230                 235                 240

Asn Tyr His Thr Glu Ser Lys Ile Asp Arg Asp Lys Ser Phe Ile Leu
                245                 250                 255

Glu Glu His Met Asp Lys Ile Asn Ser Cys Phe Ser Ala Asn Thr Val
            260                 265                 270

Glu Glu Ile Ile Glu Asn Leu Gln Gln Asp Gly Ser Ser Phe Ala Leu
        275                 280                 285

Glu Gln Leu Lys Val Ile Asn Lys Met Ser Pro Thr Ser Leu Lys Ile
    290                 295                 300

Thr Leu Arg Gln Leu Met Glu Gly Ser Ser Lys Thr Leu Gln Glu Val
305                 310                 315                 320

Leu Thr Met Glu Tyr Arg Leu Ser Gln Ala Cys Met Arg Gly His Asp
                325                 330                 335

Phe His Glu Gly Val Arg Ala Val Leu Ile Asp Lys Asp Gln Ser Pro
            340                 345                 350

Lys Trp Lys Pro Ala Asp Leu Lys Glu Val Thr Glu Glu Asp Leu Asn
        355                 360                 365

Asn His Phe Lys Ser Leu Gly Ser Ser Asp Leu Lys Phe
    370                 375                 380
```

<210> 114
<211> 1139
<212> PRT
<213> Homo sapiens

<400> 114

```
Met Gln Thr Pro Glu Val Pro Ala Glu Arg Ser Pro Arg Arg Arg Ser
1               5                  10                  15

Ile Ser Gly Thr Ser Thr Ser Glu Lys Pro Asn Ser Met Asp Thr Ala
            20                  25                  30

Asn Thr Ser Pro Phe Lys Val Pro Gly Phe Phe Ser Lys Arg Leu Lys
        35                  40                  45
```

```
Gly Ser Ile Lys Arg Thr Lys Ser Gln Ser Lys Leu Asp Arg Asn Thr
 50                  55                  60

Ser Phe Arg Leu Pro Ser Leu Arg Ser Thr Asp Asp Arg Ser Arg Gly
65                  70                  75                  80

Leu Pro Lys Leu Lys Glu Ser Arg Ser His Glu Ser Leu Leu Ser Pro
                85                  90                  95

Cys Ser Thr Val Glu Cys Leu Asp Leu Gly Arg Gly Glu Pro Val Ser
            100                 105                 110

Val Lys Pro Leu His Ser Ser Ile Leu Gly Gln Asp Phe Cys Phe Glu
        115                 120                 125

Val Thr Tyr Leu Ser Gly Ser Lys Cys Phe Ser Cys Asn Ser Ala Ser
    130                 135                 140

Glu Arg Asp Lys Trp Met Glu Asn Leu Arg Arg Thr Val Gln Pro Asn
145                 150                 155                 160

Lys Asp Asn Cys Arg Arg Ala Glu Asn Val Leu Arg Leu Trp Ile Ile
                165                 170                 175

Glu Ala Lys Asp Leu Ala Pro Lys Lys Lys Tyr Phe Cys Glu Leu Cys
            180                 185                 190

Leu Asp Asp Thr Leu Phe Ala Arg Thr Thr Ser Lys Thr Lys Ala Asp
        195                 200                 205

Asn Ile Phe Trp Gly Glu His Phe Glu Phe Phe Ser Leu Pro Pro Leu
    210                 215                 220

His Ser Ile Thr Val His Ile Tyr Lys Asp Val Glu Lys Lys Lys Lys
225                 230                 235                 240

Lys Asp Lys Asn Asn Tyr Val Gly Leu Val Asn Ile Pro Thr Ala Ser
                245                 250                 255

Val Thr Gly Arg Gln Phe Val Glu Lys Trp Tyr Pro Val Ser Thr Pro
            260                 265                 270

Thr Pro Asn Lys Gly Lys Thr Gly Gly Pro Ser Ile Arg Ile Lys Ser
        275                 280                 285

Arg Phe Gln Thr Ile Thr Ile Leu Pro Met Glu Gln Tyr Lys Glu Phe
    290                 295                 300

Ala Glu Phe Val Thr Ser Asn Tyr Thr Met Leu Cys Ser Val Leu Glu
305                 310                 315                 320

Pro Val Ile Ser Val Arg Asn Lys Glu Glu Leu Ala Cys Ala Leu Val
                325                 330                 335

His Ile Leu Gln Ser Thr Gly Arg Ala Lys Asp Phe Leu Thr Asp Leu
            340                 345                 350

Val Met Ser Glu Val Asp Arg Cys Gly Glu His Asp Val Leu Ile Phe
```



```
        355                 360                 365

Arg Glu Asn Thr Ile Ala Thr Lys Ser Ile Glu Glu Tyr Leu Lys Leu
    370                 375                 380

Val Gly Gln Gln Tyr Leu His Asp Ala Leu Gly Glu Phe Ile Lys Ala
385                 390                 395                 400

Leu Tyr Glu Ser Asp Glu Asn Cys Glu Val Asp Pro Ser Lys Cys Ser
                405                 410                 415

Ser Ser Glu Leu Ile Asp His Gln Ser Asn Leu Lys Met Cys Cys Glu
            420                 425                 430

Leu Ala Phe Cys Lys Ile Ile Asn Ser Tyr Cys Val Phe Pro Arg Glu
        435                 440                 445

Leu Lys Glu Val Phe Ala Ser Trp Lys Gln Gln Cys Leu Asn Arg Gly
    450                 455                 460

Lys Gln Asp Ile Ser Glu Arg Leu Ile Ser Ala Ser Leu Phe Leu Arg
465                 470                 475                 480

Phe Leu Cys Pro Ala Ile Met Ser Pro Ser Leu Phe Asn Leu Met Gln
                485                 490                 495

Glu Tyr Pro Asp Asp Arg Thr Ser Arg Thr Leu Thr Leu Ile Ala Lys
            500                 505                 510

Val Ile Gln Asn Leu Ala Asn Phe Ala Lys Phe Gly Asn Lys Glu Glu
        515                 520                 525

Tyr Met Ala Phe Met Asn Asp Phe Leu Glu His Glu Trp Gly Gly Met
    530                 535                 540

Lys Arg Phe Leu Leu Glu Ile Ser Asn Pro Asp Thr Ile Ser Asn Thr
545                 550                 555                 560

Pro Gly Phe Asp Gly Tyr Ile Asp Leu Gly Arg Glu Leu Ser Val Leu
                565                 570                 575

His Ser Leu Leu Trp Glu Val Val Ser Gln Leu Asp Lys Gly Glu Asn
            580                 585                 590

Ser Phe Leu Gln Ala Thr Val Ala Lys Leu Gly Pro Leu Pro Arg Val
        595                 600                 605

Leu Ala Asp Ile Thr Lys Ser Leu Thr Asn Pro Thr Pro Ile Gln Gln
    610                 615                 620

Gln Leu Arg Arg Phe Thr Glu His Asn Ser Ser Pro Asn Val Ser Gly
625                 630                 635                 640

Ser Leu Ser Ser Gly Leu Gln Lys Ile Phe Glu Asp Pro Thr Asp Ser
                645                 650                 655

Asp Leu His Lys Leu Lys Ser Pro Ser Gln Asp Asn Thr Asp Ser Tyr
            660                 665                 670
```

```
Phe Arg Gly Lys Thr Leu Leu Leu Val Gln Gln Ala Ser Ser Gln Ser
        675                 680                 685

Met Thr Tyr Ser Glu Lys Asp Glu Arg Glu Ser Ser Leu Pro Asn Gly
    690                 695                 700

Arg Ser Val Ser Leu Met Asp Leu Gln Asp Thr His Ala Ala Gln Val
705                 710                 715                 720

Glu His Ala Ser Val Met Leu Asp Val Pro Ile Arg Leu Thr Gly Ser
                725                 730                 735

Gln Leu Ser Ile Thr Gln Val Ala Ser Ile Lys Gln Leu Arg Glu Thr
            740                 745                 750

Gln Ser Thr Pro Gln Ser Ala Pro Gln Val Arg Arg Pro Leu His Pro
        755                 760                 765

Ala Leu Asn Gln Pro Gly Gly Leu Gln Pro Leu Ser Phe Gln Asn Pro
    770                 775                 780

Val Tyr His Leu Asn Asn Pro Ile Pro Ala Met Pro Lys Ala Ser Ile
785                 790                 795                 800

Asp Ser Ser Leu Glu Asn Leu Ser Thr Ala Ser Ser Arg Ser Gln Ser
                805                 810                 815

Asn Ser Glu Asp Phe Lys Leu Ser Gly Pro Ser Asn Ser Ser Met Glu
            820                 825                 830

Asp Phe Thr Lys Arg Ser Thr Gln Ser Glu Asp Phe Ser Arg Arg His
        835                 840                 845

Thr Val Pro Asp Arg His Ile Pro Leu Ala Leu Pro Arg Gln Asn Ser
    850                 855                 860

Thr Gly Gln Ala Gln Ile Arg Lys Val Asp Gln Gly Gly Leu Gly Ala
865                 870                 875                 880

Arg Ala Lys Ala Pro Pro Ser Leu Pro His Ser Ala Ser Leu Arg Ser
                885                 890                 895

Thr Gly Ser Met Ser Val Val Ser Ala Ala Leu Val Ala Glu Pro Val
            900                 905                 910

Gln Asn Gly Ser Arg Ser Arg Gln Gln Ser Ser Ser Ser Arg Glu Ser
        915                 920                 925

Pro Val Pro Lys Val Arg Ala Ile Gln Arg Gln Gln Thr Gln Gln Val
    930                 935                 940

Gln Ser Pro Val Asp Ser Ala Thr Met Ser Pro Val Glu Arg Thr Ala
945                 950                 955                 960

Ala Trp Val Leu Asn Asn Gly Gln Tyr Glu Glu Asp Val Glu Glu Thr
                965                 970                 975

Glu Gln Asn Leu Asp Glu Ala Lys His Ala Glu Lys Tyr Glu Gln Glu
            980                 985                 990
```



```
Ile Thr Lys Leu Lys Glu Arg Leu  Arg Val Ser Ser Arg  Arg Leu Glu
        995                 1000                1005

Glu Tyr  Glu Arg Arg Leu Leu  Val Gln Glu Gln Gln  Met Gln Lys
    1010                1015                1020

Leu Leu  Leu Glu Tyr Lys Ala  Arg Leu Glu Asp Ser  Glu Glu Arg
    1025                1030                1035

Leu Arg  Arg Gln Gln Glu Glu  Lys Asp Ser Gln Met  Lys Ser Ile
    1040                1045                1050

Ile Ser  Arg Leu Met Ala Val  Glu Glu Glu Leu Lys  Lys Asp His
    1055                1060                1065

Ala Glu  Met Gln Ala Val Ile  Asp Ala Lys Gln Lys  Ile Ile Asp
    1070                1075                1080

Ala Gln  Glu Lys Arg Ile Val  Ser Leu Asp Ser Ala  Asn Thr Arg
    1085                1090                1095

Leu Met  Ser Ala Leu Thr Gln  Val Lys Glu Arg Tyr  Ser Met Gln
    1100                1105                1110

Val Arg  Asn Gly Ile Ser Pro  Thr Asn Pro Thr Lys  Leu Ser Ile
    1115                1120                1125

Thr Glu  Asn Gly Glu Phe Lys  Asn Ser Ser Cys
    1130                1135
```

<210> 115
<211> 165
<212> PRT
<213> Homo sapiens

<400> 115

```
Met Thr Leu Glu Glu Phe Ser Ala Gly Glu Gln Lys Thr Glu Arg Met
1               5                   10                  15

Asp Lys Val Gly Asp Ala Leu Glu Glu Val Leu Ser Lys Ala Leu Ser
            20                  25                  30

Gln Arg Thr Ile Thr Val Gly Val Tyr Glu Ala Ala Lys Leu Leu Asn
        35                  40                  45

Val Asp Pro Asp Asn Val Val Leu Cys Leu Leu Ala Ala Asp Glu Asp
    50                  55                  60

Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr Leu Ile Gln Ala
65                  70                  75                  80

Phe Cys Cys Glu Asn Asp Ile Asn Ile Leu Arg Val Ser Asn Pro Gly
                85                  90                  95

Arg Leu Ala Glu Leu Leu Leu Leu Glu Thr Asp Ala Gly Pro Ala Ala
            100                 105                 110

Ser Glu Gly Ala Glu Gln Pro Pro Asp Leu His Cys Val Leu Val Thr
        115                 120                 125
```

```
Asn Pro His Ser Ser Gln Trp Lys Asp Pro Ala Leu Ser Gln Leu Ile
    130                 135                 140

Cys Phe Cys Arg Glu Ser Arg Tyr Met Asp Gln Trp Val Pro Val Ile
145                 150                 155                 160

Asn Leu Pro Glu Arg
                165
```

<210> 116
<211> 1163
<212> PRT
<213> Homo sapiens

<400> 116

```
Met Thr Arg Thr Arg Ala Ala Leu Leu Leu Phe Thr Ala Leu Ala Thr
1               5                   10                  15

Ser Leu Gly Phe Asn Leu Asp Thr Glu Glu Leu Thr Ala Phe Arg Val
            20                  25                  30

Asp Ser Ala Gly Phe Gly Asp Ser Val Val Gln Tyr Ala Asn Ser Trp
        35                  40                  45

Val Val Val Gly Ala Pro Gln Lys Ile Thr Ala Ala Asn Gln Thr Gly
    50                  55                  60

Gly Leu Tyr Gln Cys Gly Tyr Ser Thr Gly Ala Cys Glu Pro Ile Gly
65                  70                  75                  80

Leu Gln Val Pro Pro Glu Ala Val Asn Met Ser Leu Gly Leu Ser Leu
                85                  90                  95

Ala Ser Thr Thr Ser Pro Ser Gln Leu Leu Ala Cys Gly Pro Thr Val
            100                 105                 110

His His Glu Cys Gly Arg Asn Met Tyr Leu Thr Gly Leu Cys Phe Leu
        115                 120                 125

Leu Gly Pro Thr Gln Leu Thr Gln Arg Leu Pro Val Ser Arg Gln Glu
    130                 135                 140

Cys Pro Arg Gln Glu Gln Asp Ile Val Phe Leu Ile Asp Gly Ser Gly
145                 150                 155                 160

Ser Ile Ser Ser Arg Asn Phe Ala Thr Met Met Asn Phe Val Arg Ala
                165                 170                 175

Val Ile Ser Gln Phe Gln Arg Pro Ser Thr Gln Phe Ser Leu Met Gln
            180                 185                 190

Phe Ser Asn Lys Phe Gln Thr His Leu Thr Phe Glu Glu Phe Arg Arg
        195                 200                 205

Thr Ser Asn Pro Leu Ser Leu Leu Ala Ser Val His Gln Leu Gln Gly
    210                 215                 220

Phe Thr Tyr Thr Ala Thr Ala Ile Gln Asn Val Val His Arg Leu Phe
225                 230                 235                 240
```



```
His Ala Ser Tyr Gly Ala Arg Arg Asp Ala Thr Lys Ile Leu Ile Val
                245                 250                 255

Ile Thr Asp Gly Lys Lys Glu Gly Asp Thr Leu Asp Tyr Lys Asp Val
            260                 265                 270

Ile Pro Met Ala Asp Ala Ala Gly Ile Ile Arg Tyr Ala Ile Gly Val
        275                 280                 285

Gly Leu Ala Phe Gln Asn Arg Asn Ser Trp Lys Glu Leu Asn Asp Ile
    290                 295                 300

Ala Ser Lys Pro Ser Gln Glu His Ile Phe Lys Val Glu Asp Phe Asp
305                 310                 315                 320

Ala Leu Lys Asp Ile Gln Thr Gln Leu Arg Glu Lys Ile Phe Pro Ile
                325                 330                 335

Glu Gly Thr Glu Thr Thr Ser Ser Ser Ser Phe Glu Leu Glu Met Ala
            340                 345                 350

Gln Glu Gly Phe Ser Ala Val Phe Thr Pro Asp Gly Pro Val Leu Gly
        355                 360                 365

Ala Val Gly Ser Phe Thr Trp Ser Gly Gly Ala Phe Leu Tyr Pro Pro
    370                 375                 380

Asn Met Ser Pro Thr Phe Ile Asn Met Ser Gln Glu Asn Val Asp Met
385                 390                 395                 400

Arg Asp Ser Tyr Leu Gly Tyr Ser Thr Glu Leu Ala Leu Trp Lys Gly
                405                 410                 415

Val Gln Ser Leu Val Leu Gly Ala Pro Arg Tyr Gln His Thr Gly Lys
            420                 425                 430

Ala Val Ile Phe Thr Gln Val Ser Arg Gln Trp Arg Met Lys Ala Glu
        435                 440                 445

Val Thr Gly Thr Gln Ile Gly Ser Tyr Phe Gly Pro Ser Leu Cys Ser
    450                 455                 460

Val Asp Val Asp Ser Asp Gly Ser Thr Asp Leu Val Leu Ile Gly Pro
465                 470                 475                 480

Pro His Tyr Tyr Glu Gln Thr Arg Gly Ala Gln Val Ser Val Cys Pro
                485                 490                 495

Leu Pro Arg Gly Trp Arg Arg Trp Trp Cys Asp Ala Val Leu Tyr Gly
            500                 505                 510

Glu Gln Gly His Pro Trp Gly Arg Phe Gly Ala Ala Leu Thr Val Leu
        515                 520                 525

Gly Asp Val Asn Gly Asp Lys Leu Thr Asp Val Val Ile Gly Ala Pro
    530                 535                 540

Gly Glu Glu Glu Asn Arg Gly Ala Val Tyr Leu Phe His Gly Val Leu
545                 550                 555                 560
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Gly Pro Ser Ile Ser Pro Ser His Ser Gln Arg Ile Ala Gly Ser Gln
                565                 570                 575

Leu Ser Ser Arg Leu Gln Tyr Phe Gly Gln Ala Leu Ser Gly Gly Gln
            580                 585                 590

Asp Leu Thr Gln Asp Gly Leu Val Asp Leu Ala Val Gly Ala Arg Gly
        595                 600                 605

Gln Val Leu Leu Leu Arg Thr Arg Pro Val Leu Trp Val Gly Val Ser
    610                 615                 620

Met Gln Phe Ile Pro Ala Glu Ile Pro Arg Ser Ala Phe Glu Cys Arg
625                 630                 635                 640

Glu Gln Val Val Ser Glu Gln Thr Leu Val Gln Ser Asn Ile Cys Leu
                645                 650                 655

Tyr Ile Asp Lys Arg Ser Lys Asn Leu Leu Gly Ser Arg Asp Leu Gln
            660                 665                 670

Ser Ser Val Thr Leu Asp Leu Ala Leu Asp Pro Gly Arg Leu Ser Pro
        675                 680                 685

Arg Ala Thr Phe Gln Glu Thr Lys Asn Arg Ser Leu Ser Arg Val Arg
    690                 695                 700

Val Leu Gly Leu Lys Ala His Cys Glu Asn Phe Asn Leu Leu Leu Pro
705                 710                 715                 720

Ser Cys Val Glu Asp Ser Val Thr Pro Ile Thr Leu Arg Leu Asn Phe
                725                 730                 735

Thr Leu Val Gly Lys Pro Leu Leu Ala Phe Arg Asn Leu Arg Pro Met
            740                 745                 750

Leu Ala Ala Asp Ala Gln Arg Tyr Phe Thr Ala Ser Leu Pro Phe Glu
        755                 760                 765

Lys Asn Cys Gly Ala Asp His Ile Cys Gln Asp Asn Leu Gly Ile Ser
    770                 775                 780

Phe Ser Phe Pro Gly Leu Lys Ser Leu Leu Val Gly Ser Asn Leu Glu
785                 790                 795                 800

Leu Asn Ala Glu Val Met Val Trp Asn Asp Gly Glu Asp Ser Tyr Gly
                805                 810                 815

Thr Thr Ile Thr Phe Ser His Pro Ala Gly Leu Ser Tyr Arg Tyr Val
            820                 825                 830

Ala Glu Gly Gln Lys Gln Gly Gln Leu Arg Ser Leu His Leu Thr Cys
        835                 840                 845

Asp Ser Ala Pro Val Gly Ser Gln Gly Thr Trp Ser Thr Ser Cys Arg
    850                 855                 860

Ile Asn His Leu Ile Phe Arg Gly Gly Ala Gln Ile Thr Phe Leu Ala
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865                 870                 875                 880

Thr Phe Asp Val Ser Pro Lys Ala Val Leu Gly Asp Arg Leu Leu Leu
                885                 890                 895

Thr Ala Asn Val Ser Ser Glu Asn Asn Thr Pro Arg Thr Ser Lys Thr
            900                 905                 910

Thr Phe Gln Leu Glu Leu Pro Val Lys Tyr Ala Val Tyr Thr Val Val
        915                 920                 925

Ser Ser His Glu Gln Phe Thr Lys Tyr Leu Asn Phe Ser Glu Ser Glu
    930                 935                 940

Glu Lys Glu Ser His Val Ala Met His Arg Tyr Gln Val Asn Asn Leu
945                 950                 955                 960

Gly Gln Arg Asp Leu Pro Val Ser Ile Asn Phe Trp Val Pro Val Glu
                965                 970                 975

Leu Asn Gln Glu Ala Val Trp Met Asp Val Glu Val Ser Leu Pro Gln
            980                 985                 990

Asn Pro Ser Leu Arg Cys Ser Ser Glu Lys Ile Ala Gly Pro Ala Ser
        995                 1000                1005

Asp Phe Leu Ala His Ile Gln Lys Asn Pro Val Leu Asp Cys Ser
    1010                1015                1020

Ile Ala Gly Cys Leu Arg Phe Arg Cys Asp Val Pro Ser Phe Ser
    1025                1030                1035

Val Gln Glu Glu Leu Asp Phe Thr Leu Lys Gly Asn Leu Ser Phe
    1040                1045                1050

Gly Trp Val Arg Gln Ile Leu Gln Lys Lys Val Ser Val Val Ser
    1055                1060                1065

Val Ala Glu Ile Thr Phe Asp Thr Ser Val Tyr Ser Gln Leu Pro
    1070                1075                1080

Gly Gln Glu Ala Phe Met Arg Ala Gln Thr Thr Thr Val Leu Glu
    1085                1090                1095

Lys Tyr Lys Val His Asn Pro Thr Pro Leu Ile Val Gly Ser Ser
    1100                1105                1110

Ile Gly Gly Leu Leu Leu Leu Ala Leu Ile Thr Ala Val Leu Tyr
    1115                1120                1125

Lys Val Gly Phe Phe Lys Arg Gln Tyr Lys Glu Met Met Glu Glu
    1130                1135                1140

Ala Asn Gly Gln Ile Ala Pro Glu Asn Gly Thr Gln Thr Pro Ser
    1145                1150                1155

Pro Pro Ser Glu Lys
    1160
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<210> 117
<211> 335
<212> PRT
<213> Homo sapiens

<400> 117

Met Leu Gly Ile Trp Thr Leu Leu Pro Leu Val Leu Thr Ser Val Ala
1 5 10 15

Arg Leu Ser Ser Lys Ser Val Asn Ala Gln Val Thr Asp Ile Asn Ser
20 25 30

Lys Gly Leu Glu Leu Arg Lys Thr Val Thr Thr Val Glu Thr Gln Asn
35 40 45

Leu Glu Gly Leu His His Asp Gly Gln Phe Cys His Lys Pro Cys Pro
50 55 60

Pro Gly Glu Arg Lys Ala Arg Asp Cys Thr Val Asn Gly Asp Glu Pro
65 70 75 80

Asp Cys Val Pro Cys Gln Glu Gly Lys Glu Tyr Thr Asp Lys Ala His
85 90 95

Phe Ser Ser Lys Cys Arg Arg Cys Arg Leu Cys Asp Glu Gly His Gly
100 105 110

Leu Glu Val Glu Ile Asn Cys Thr Arg Thr Gln Asn Thr Lys Cys Arg
115 120 125

Cys Lys Pro Asn Phe Phe Cys Asn Ser Thr Val Cys Glu His Cys Asp
130 135 140

Pro Cys Thr Lys Cys Glu His Gly Ile Ile Lys Glu Cys Thr Leu Thr
145 150 155 160

Ser Asn Thr Lys Cys Lys Glu Glu Gly Ser Arg Ser Asn Leu Gly Trp
165 170 175

Leu Cys Leu Leu Leu Leu Pro Ile Pro Leu Ile Val Trp Val Lys Arg
180 185 190

Lys Glu Val Gln Lys Thr Cys Arg Lys His Arg Lys Glu Asn Gln Gly
195 200 205

Ser His Glu Ser Pro Thr Leu Asn Pro Glu Thr Val Ala Ile Asn Leu
210 215 220

Ser Asp Val Asp Leu Ser Lys Tyr Ile Thr Thr Ile Ala Gly Val Met
225 230 235 240

Thr Leu Ser Gln Val Lys Gly Phe Val Arg Lys Asn Gly Val Asn Glu
245 250 255

Ala Lys Ile Asp Glu Ile Lys Asn Asp Asn Val Gln Asp Thr Ala Glu
260 265 270

Gln Lys Val Gln Leu Leu Arg Asn Trp His Gln Leu His Gly Lys Lys
275 280 285

Glu Ala Tyr Asp Thr Leu Ile Lys Asp Leu Lys Lys Ala Asn Leu Cys
290 295 300

Thr Leu Ala Glu Lys Ile Gln Thr Ile Ile Leu Lys Asp Ile Thr Ser
305 310 315 320

Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val
325 330 335

<210> 118
<211> 1251
<212> PRT
<213> Homo sapiens

<400> 118

Met Glu Leu Ser Asp Val Arg Cys Leu Thr Gly Ser Glu Glu Leu Tyr
1 5 10 15

Thr Ile His Pro Thr Pro Pro Ala Gly Asp Gly Arg Ser Ala Ser Arg
20 25 30

Pro Gln Arg Leu Leu Trp Gln Thr Ala Val Arg His Ile Thr Glu Gln
35 40 45

Arg Phe Ile His Gly His Arg Gly Gly Ser Gly Ser Gly Ser Gly Gly
50 55 60

Ser Gly Lys Ala Ser Asp Pro Ala Gly Gly Gly Pro Asn His His Ala
65 70 75 80

Pro Gln Leu Ser Gly Asp Ser Ala Leu Pro Leu Tyr Ser Leu Gly Pro
85 90 95

Gly Glu Arg Ala His Ser Thr Cys Gly Thr Lys Val Phe Pro Glu Arg
100 105 110

Ser Gly Ser Gly Ser Ala Ser Gly Ser Gly Gly Gly Gly Asp Leu Gly
115 120 125

Phe Leu His Leu Asp Cys Ala Pro Ser Asn Ser Asp Phe Phe Leu Asn
130 135 140

Gly Gly Tyr Ser Tyr Arg Gly Val Ile Phe Pro Thr Leu Arg Asn Ser
145 150 155 160

Phe Lys Ser Arg Asp Leu Glu Arg Leu Tyr Gln Arg Tyr Phe Leu Gly
165 170 175

Gln Arg Arg Lys Ser Glu Val Val Met Asn Val Leu Asp Val Leu Thr
180 185 190

Lys Leu Thr Leu Leu Val Leu His Leu Ser Leu Ala Ser Ala Pro Met
195 200 205

Asp Pro Leu Lys Gly Ile Leu Leu Gly Phe Phe Thr Gly Ile Glu Val
210 215 220

Val Ile Cys Ala Leu Val Val Val Arg Lys Asp Thr Thr Ser His Thr
225 230 235 240

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Tyr Leu Gln Tyr Ser Gly Val Val Thr Trp Val Ala Met Thr Thr Gln
                245                 250                 255

Ile Leu Ala Ala Gly Leu Gly Tyr Gly Leu Leu Gly Asp Gly Ile Gly
            260                 265                 270

Tyr Val Leu Phe Thr Leu Phe Ala Thr Tyr Ser Met Leu Pro Leu Pro
        275                 280                 285

Leu Thr Trp Ala Ile Leu Ala Gly Leu Gly Thr Ser Leu Leu Gln Val
    290                 295                 300

Ile Leu Gln Val Val Ile Pro Arg Leu Ala Val Ile Ser Ile Asn Gln
305                 310                 315                 320

Val Val Ala Gln Ala Val Leu Phe Met Cys Met Asn Thr Ala Gly Ile
                325                 330                 335

Phe Ile Ser Tyr Leu Ser Asp Arg Ala Gln Arg Gln Ala Phe Leu Glu
            340                 345                 350

Thr Arg Arg Cys Val Glu Ala Arg Leu Arg Leu Glu Thr Glu Asn Gln
        355                 360                 365

Arg Gln Glu Arg Leu Val Leu Ser Val Leu Pro Arg Phe Val Val Leu
    370                 375                 380

Glu Met Ile Asn Asp Met Thr Asn Val Glu Asp Glu His Leu Gln His
385                 390                 395                 400

Gln Phe His Arg Ile Tyr Ile His Arg Tyr Glu Asn Val Ser Ile Leu
                405                 410                 415

Phe Ala Asp Val Lys Gly Phe Thr Asn Leu Ser Thr Thr Leu Ser Ala
            420                 425                 430

Gln Glu Leu Val Arg Met Leu Asn Glu Leu Phe Ala Arg Phe Asp Arg
        435                 440                 445

Leu Ala His Glu His His Cys Leu Arg Ile Lys Ile Leu Gly Asp Cys
    450                 455                 460

Tyr Tyr Cys Val Ser Gly Leu Pro Glu Pro Arg Gln Asp His Ala His
465                 470                 475                 480

Cys Cys Val Glu Met Gly Leu Ser Met Ile Lys Thr Ile Arg Tyr Val
                485                 490                 495

Arg Ser Arg Thr Lys His Asp Val Asp Met Arg Ile Gly Ile His Ser
            500                 505                 510

Gly Ser Val Leu Cys Gly Val Leu Gly Leu Arg Lys Trp Gln Phe Asp
        515                 520                 525

Val Trp Ser Trp Asp Val Asp Ile Ala Asn Lys Leu Glu Ser Gly Gly
    530                 535                 540

Ile Pro Gly Arg Ile His Ile Ser Lys Ala Thr Leu Asp Cys Leu Asn
545                 550                 555                 560
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Gly Asp Tyr Asn Val Glu Glu Gly His Gly Lys Glu Arg Asn Glu Phe
                565                 570                 575

Leu Arg Lys His Asn Ile Glu Thr Tyr Leu Ile Lys Gln Pro Glu Asp
            580                 585                 590

Ser Leu Leu Ser Leu Pro Glu Asp Ile Val Lys Glu Ser Val Ser Ser
        595                 600                 605

Ser Asp Arg Arg Asn Ser Gly Ala Thr Phe Thr Glu Gly Ser Trp Ser
    610                 615                 620

Pro Glu Leu Pro Phe Asp Asn Ile Val Gly Lys Gln Asn Thr Leu Ala
625                 630                 635                 640

Ala Leu Thr Arg Asn Ser Ile Asn Leu Leu Pro Asn His Leu Ala Gln
                645                 650                 655

Ala Leu His Val Gln Ser Gly Pro Glu Glu Ile Asn Lys Arg Ile Glu
            660                 665                 670

His Thr Ile Asp Leu Arg Ser Gly Asp Lys Leu Arg Arg Glu His Ile
        675                 680                 685

Lys Pro Phe Ser Leu Met Phe Lys Asp Ser Ser Leu Glu His Lys Tyr
    690                 695                 700

Ser Gln Met Arg Asp Glu Val Phe Lys Ser Asn Leu Val Cys Ala Phe
705                 710                 715                 720

Ile Val Leu Leu Phe Ile Thr Ala Ile Gln Ser Leu Leu Pro Ser Ser
                725                 730                 735

Arg Val Met Pro Met Thr Ile Gln Phe Ser Ile Leu Ile Met Leu His
            740                 745                 750

Ser Ala Leu Val Leu Ile Thr Thr Ala Glu Asp Tyr Lys Cys Leu Pro
        755                 760                 765

Leu Ile Leu Arg Lys Thr Cys Cys Trp Ile Asn Glu Thr Tyr Leu Ala
    770                 775                 780

Arg Asn Val Ile Ile Phe Ala Ser Ile Leu Ile Asn Phe Leu Gly Ala
785                 790                 795                 800

Ile Leu Asn Ile Leu Trp Cys Asp Phe Asp Lys Ser Ile Pro Leu Lys
                805                 810                 815

Asn Leu Thr Phe Asn Ser Ser Ala Val Phe Thr Asp Ile Cys Ser Tyr
            820                 825                 830

Pro Glu Tyr Phe Val Phe Thr Gly Val Leu Ala Met Val Thr Cys Ala
        835                 840                 845

Val Phe Leu Arg Leu Asn Ser Val Leu Lys Leu Ala Val Leu Leu Ile
    850                 855                 860

Met Ile Ala Ile Tyr Ala Leu Leu Thr Glu Thr Val Tyr Ala Gly Leu
865                 870                 875                 880
```

```
Phe Leu Arg Tyr Asp Asn Leu Asn His Ser Gly Glu Asp Phe Leu Gly
                885                 890                 895

Thr Lys Glu Val Ser Leu Leu Leu Met Ala Met Phe Leu Leu Ala Val
            900                 905                 910

Phe Tyr His Gly Gln Gln Leu Glu Tyr Thr Ala Arg Leu Asp Phe Leu
        915                 920                 925

Trp Arg Val Gln Ala Lys Glu Glu Ile Asn Glu Met Lys Glu Leu Arg
    930                 935                 940

Glu His Asn Glu Asn Met Leu Arg Asn Ile Leu Pro Ser His Val Ala
945                 950                 955                 960

Arg His Phe Leu Glu Lys Asp Arg Asp Asn Glu Glu Leu Tyr Ser Gln
                965                 970                 975

Ser Tyr Asp Ala Val Gly Val Met Phe Ala Ser Ile Pro Gly Phe Ala
            980                 985                 990

Asp Phe Tyr Ser Gln Thr Glu Met  Asn Asn Gln Gly Val  Glu Cys Leu
        995                 1000                1005

Arg Leu  Leu Asn Glu Ile Ile  Ala Asp Phe Asp Glu  Leu Leu Gly
    1010                1015                1020

Glu Asp  Arg Phe Gln Asp Ile  Glu Lys Ile Lys Thr  Ile Gly Ser
    1025                1030                1035

Thr Tyr  Met Ala Val Ser Gly  Leu Ser Pro Glu Lys  Gln Gln Cys
    1040                1045                1050

Glu Asp  Lys Trp Gly His Leu  Cys Ala Leu Ala Asp  Phe Ser Leu
    1055                1060                1065

Ala Leu  Thr Glu Ser Ile Gln  Glu Ile Asn Lys His  Ser Phe Asn
    1070                1075                1080

Asn Phe  Glu Leu Arg Ile Gly  Ile Ser His Gly Ser  Val Val Ala
    1085                1090                1095

Gly Val  Ile Gly Ala Lys Lys  Pro Gln Tyr Asp Ile  Trp Gly Lys
    1100                1105                1110

Thr Val  Asn Leu Ala Ser Arg  Met Asp Ser Thr Gly  Val Ser Gly
    1115                1120                1125

Arg Ile  Gln Val Pro Glu Glu  Thr Tyr Leu Ile Leu  Lys Asp Gln
    1130                1135                1140

Gly Phe  Ala Phe Asp Tyr Arg  Gly Glu Ile Tyr Val  Lys Gly Ile
    1145                1150                1155

Ser Glu  Gln Glu Gly Lys Ile  Lys Thr Tyr Phe Leu  Leu Gly Arg
    1160                1165                1170

Val Gln  Pro Asn Pro Phe Ile  Leu Pro Pro Arg Arg  Leu Pro Gly
```



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    1175                1180                1185

Gln Tyr  Ser Leu Ala Ala Val  Val Leu Gly Leu Val  Gln Ser Leu
    1190                1195                1200

Asn Arg  Gln Arg Gln Lys Gln  Leu Leu Asn Glu Asn  Asn Asn Thr
    1205                1210                1215

Gly Ile  Ile Lys Gly His Tyr  Asn Arg Arg Thr Leu  Leu Ser Pro
    1220                1225                1230

Ser Gly  Thr Glu Pro Gly Ala  Gln Ala Glu Gly Thr  Asp Lys Ser
    1235                1240                1245

Asp Leu  Pro
    1250
```

<210> 119
<211> 143
<212> PRT
<213> Homo sapiens

<400> 119

```
Met Gly Lys Cys Arg Gly Leu Arg Thr Ala Arg Lys Leu Arg Ser His
1               5                   10                  15

Arg Arg Asp Gln Lys Trp His Asp Lys Gln Tyr Lys Lys Ala His Leu
            20                  25                  30

Gly Thr Ala Leu Lys Ala Asn Pro Phe Gly Gly Ala Ser His Ala Lys
        35                  40                  45

Gly Ile Val Leu Glu Lys Val Gly Val Glu Ala Lys Gln Pro Asn Ser
    50                  55                  60

Ala Ile Arg Lys Cys Val Arg Val Gln Leu Ile Lys Asn Gly Lys Lys
65                  70                  75                  80

Ile Thr Ala Phe Val Pro Asn Asp Gly Cys Leu Asn Phe Ile Glu Glu
                85                  90                  95

Asn Asp Glu Val Leu Val Ala Gly Phe Gly Arg Lys Gly His Ala Val
            100                 105                 110

Gly Asp Ile Pro Gly Val Arg Phe Lys Val Val Lys Val Ala Asn Val
        115                 120                 125

Ser Leu Leu Ala Leu Tyr Lys Gly Lys Lys Glu Arg Pro Arg Ser
    130                 135                 140
```

<210> 120
<211> 144
<212> PRT
<213> Homo sapiens

<400> 120

```
Met Ala Phe Thr Phe Ala Ala Phe Cys Tyr Met Leu Ala Leu Leu Leu
1               5                   10                  15

Thr Ala Ala Leu Ile Phe Phe Ala Ile Trp His Ile Ile Ala Phe Asp
            20                  25                  30
```

Glu Leu Lys Thr Asp Tyr Lys Asn Pro Ile Asp Gln Cys Asn Thr Leu
35 40 45

Asn Pro Leu Val Leu Pro Glu Tyr Leu Ile His Ala Phe Phe Cys Val
50 55 60

Met Phe Leu Cys Ala Ala Glu Trp Leu Thr Leu Gly Leu Asn Met Pro
65 70 75 80

Leu Leu Ala Tyr His Ile Trp Arg Tyr Met Ser Arg Pro Val Met Ser
85 90 95

Gly Pro Gly Leu Tyr Asp Pro Thr Thr Ile Met Asn Ala Asp Ile Leu
100 105 110

Ala Tyr Cys Gln Lys Glu Gly Trp Cys Lys Leu Ala Phe Tyr Leu Leu
115 120 125

Ala Phe Phe Tyr Tyr Leu Tyr Gly Met Ile Tyr Val Leu Val Ser Ser
130 135 140

<210> 121
<211> 1516
<212> PRT
<213> Homo sapiens

<400> 121

Met Ala Pro Ala Lys Ala Thr Asn Val Val Arg Leu Leu Leu Gly Ser
1 5 10 15

Thr Ala Leu Trp Leu Ser Gln Leu Gly Ser Gly Thr Val Ala Ala Ser
20 25 30

Lys Ser Val Thr Ala His Leu Ala Ala Lys Trp Pro Glu Thr Pro Leu
35 40 45

Leu Leu Glu Ala Ser Glu Phe Met Ala Glu Glu Ser Asn Glu Lys Phe
50 55 60

Trp Gln Phe Leu Glu Thr Val Gln Glu Leu Ala Ile Tyr Lys Gln Thr
65 70 75 80

Glu Ser Asp Tyr Ser Tyr Tyr Asn Leu Ile Leu Lys Lys Ala Gly Gln
85 90 95

Phe Leu Asp Asn Leu His Ile Asn Leu Leu Lys Phe Ala Phe Ser Ile
100 105 110

Arg Ala Tyr Ser Pro Ala Ile Gln Met Phe Gln Gln Ile Ala Ala Asp
115 120 125

Glu Pro Pro Pro Asp Gly Cys Asn Ala Phe Val Val Ile His Lys Lys
130 135 140

His Thr Cys Lys Ile Asn Glu Ile Lys Lys Leu Leu Lys Lys Ala Ala
145 150 155 160

Ser Arg Thr Arg Pro Tyr Leu Phe Lys Gly Asp His Lys Phe Pro Thr
165 170 175

Asn Lys Glu Asn Leu Pro Val Val Ile Leu Tyr Ala Glu Met Gly Thr
180 185 190

Arg Thr Phe Ser Ala Phe His Lys Val Leu Ser Glu Lys Ala Gln Asn
195 200 205

Glu Glu Ile Leu Tyr Val Leu Arg His Tyr Ile Gln Lys Pro Ser Ser
210 215 220

Arg Lys Met Tyr Leu Ser Gly Tyr Gly Val Glu Leu Ala Ile Lys Ser
225 230 235 240

Thr Glu Tyr Lys Ala Leu Asp Asp Thr Gln Val Lys Thr Val Thr Asn
245 250 255

Thr Thr Val Glu Asp Glu Thr Glu Thr Asn Glu Val Gln Gly Phe Leu
260 265 270

Phe Gly Lys Leu Lys Glu Ile Tyr Ser Asp Leu Arg Asp Asn Leu Thr
275 280 285

Ala Phe His Lys Tyr Leu Ile Glu Ser Asn Lys Gln Met Met Pro Leu
290 295 300

Lys Val Trp Glu Leu Gln Asp Leu Ser Phe Gln Ala Ala Ser Gln Ile
305 310 315 320

Met Ser Thr Pro Val Tyr Asp Ala Ile Lys Leu Met Lys Asp Ile Ser
325 330 335

Gln Asn Phe Pro Ile Lys Ala Arg Ser Leu Thr Arg Ile Ala Val Asn
340 345 350

Gln His Met Arg Glu Glu Ile Lys Glu Asn Gln Lys Asp Leu Gln Val
355 360 365

Arg Phe Lys Ile Gln Pro Gly Asp Ala Arg Leu Phe Ile Asn Gly Leu
370 375 380

Arg Val Asp Met Asp Val Tyr Asp Ala Phe Ser Ile Leu Asp Met Leu
385 390 395 400

Lys Leu Glu Gly Lys Met Met Asn Gly Leu Arg Asn Leu Gly Ile Asn
405 410 415

Gly Glu Asp Met Ser Lys Phe Leu Lys Leu Asn Ser His Ile Trp Glu
420 425 430

Tyr Thr Tyr Val Leu Asp Ile Arg His Ser Ser Ile Met Trp Ile Asn
435 440 445

Asp Leu Glu Asn Asp Asp Leu Tyr Ile Thr Trp Pro Thr Ser Cys Gln
450 455 460

Lys Leu Leu Lys Pro Val Phe Pro Gly Ser Val Pro Ser Ile Arg Arg
465 470 475 480

Asn Phe His Asn Leu Val Leu Phe Ile Asp Pro Ala Gln Glu Tyr Thr

485 490 495

Leu Asp Phe Ile Lys Leu Ala Asp Val Phe Tyr Ser His Glu Val Pro
500 505 510

Leu Arg Ile Gly Phe Val Phe Ile Leu Asn Thr Asp Asp Glu Val Asp
515 520 525

Gly Ala Asn Asp Ala Gly Val Ala Leu Trp Arg Ala Phe Asn Tyr Ile
530 535 540

Ala Glu Glu Phe Asp Ile Ser Glu Ala Phe Ile Ser Ile Val His Met
545 550 555 560

Tyr Gln Lys Val Lys Lys Asp Gln Asn Ile Leu Thr Val Asp Asn Val
565 570 575

Lys Ser Val Leu Gln Asn Thr Phe Pro His Ala Asn Ile Trp Asp Ile
580 585 590

Leu Gly Ile His Ser Lys Tyr Asp Glu Glu Arg Lys Ala Gly Ala Ser
595 600 605

Phe Tyr Lys Met Thr Gly Leu Gly Pro Leu Pro Gln Ala Leu Tyr Asn
610 615 620

Gly Glu Pro Phe Lys His Glu Glu Met Asn Ile Lys Glu Leu Lys Met
625 630 635 640

Ala Val Leu Gln Arg Met Met Asp Ala Ser Val Tyr Leu Gln Arg Glu
645 650 655

Val Phe Leu Gly Thr Leu Asn Asp Arg Thr Asn Ala Ile Asp Phe Leu
660 665 670

Met Asp Arg Asn Asn Val Val Pro Arg Ile Asn Thr Leu Ile Leu Arg
675 680 685

Thr Asn Gln Gln Tyr Leu Asn Leu Ile Ser Thr Ser Val Thr Ala Asp
690 695 700

Val Glu Asp Phe Ser Thr Phe Phe Phe Leu Asp Ser Gln Asp Lys Ser
705 710 715 720

Ala Val Ile Ala Lys Asn Met Tyr Tyr Leu Thr Gln Asp Asp Glu Ser
725 730 735

Ile Ile Ser Ala Val Thr Leu Trp Ile Ile Ala Asp Phe Asp Lys Pro
740 745 750

Ser Gly Arg Lys Leu Leu Phe Asn Ala Leu Lys His Met Lys Thr Ser
755 760 765

Val His Ser Arg Leu Gly Ile Ile Tyr Asn Pro Thr Ser Lys Ile Asn
770 775 780

Glu Glu Asn Thr Ala Ile Ser Arg Gly Ile Leu Ala Ala Phe Leu Thr
785 790 795 800

Gln Lys Asn Met Phe Leu Arg Ser Phe Leu Gly Gln Leu Ala Lys Glu
805 810 815

Glu Ile Ala Thr Thr Ile Tyr Ser Gly Asp Lys Ile Lys Thr Phe Leu
820 825 830

Ile Glu Gly Met Asp Lys Asn Ala Phe Glu Lys Lys Tyr Asn Thr Val
835 840 845

Gly Val Asn Ile Phe Arg Thr His Gln Leu Phe Cys Gln Asp Val Leu
850 855 860

Lys Leu Arg Pro Gly Glu Met Gly Ile Val Ser Asn Gly Arg Phe Leu
865 870 875 880

Gly Pro Leu Asp Glu Asp Phe Tyr Ala Glu Asp Phe Tyr Leu Leu Glu
885 890 895

Lys Ile Thr Phe Ser Asn Leu Gly Glu Lys Ile Lys Gly Ile Val Glu
900 905 910

Asn Met Gly Ile Asn Ala Asn Asn Met Ser Asp Phe Ile Met Lys Val
915 920 925

Asp Ala Leu Met Ser Ser Val Pro Lys Arg Ala Ser Arg Tyr Asp Val
930 935 940

Thr Phe Leu Arg Glu Asn His Ser Val Ile Lys Thr Asn Pro Gln Glu
945 950 955 960

Asn Asp Met Phe Phe Asn Val Ile Ala Ile Val Asp Leu Leu Ala Arg
965 970 975

Glu Ala Gln Lys Met Ala Gln Leu Leu Val Val Leu Gly Lys Ile Ile
980 985 990

Asn Leu Lys Ile Lys Leu Phe Met Asn Cys Arg Gly Arg Leu Ser Glu
995 1000 1005

Ala Pro Leu Glu Ser Phe Tyr Arg Phe Val Leu Glu Pro Glu Leu
1010 1015 1020

Met Ser Gly Ala Asn Asp Val Ser Ser Leu Gly Pro Val Ala Lys
1025 1030 1035

Phe Leu Asp Ile Pro Glu Ser Pro Leu Leu Ile Leu Asn Met Ile
1040 1045 1050

Thr Pro Glu Gly Trp Leu Val Glu Thr Val His Ser Asn Cys Asp
1055 1060 1065

Leu Asp Asn Ile His Leu Lys Asp Thr Glu Lys Thr Ala Thr Ala
1070 1075 1080

Gly Tyr Glu Leu Glu Tyr Leu Leu Leu Glu Gly Gln Cys Phe Asp
1085 1090 1095

Lys Val Thr Glu Gln Pro Pro Arg Gly Leu Gln Phe Thr Leu Gly
1100 1105 1110

Thr Lys Asn Lys Pro Ala Val Val Asp Thr Ile Val Met Ala His
1115 1120 1125

His Gly Tyr Phe Gln Leu Lys Ala Asn Pro Gly Ala Trp Ile Leu
1130 1135 1140

Arg Leu His Gln Gly Lys Ser Glu Asp Ile Tyr Gln Ile Val Gly
1145 1150 1155

His Glu Gly Thr Asp Ser Gln Ala Asp Leu Glu Asp Ile Ile Val
1160 1165 1170

Val Leu Asn Ser Phe Lys Ser Lys Ile Leu Lys Val Lys Val Lys
1175 1180 1185

Lys Glu Thr Asp Lys Ile Lys Glu Asp Ile Leu Thr Asp Glu Asp
1190 1195 1200

Glu Lys Thr Lys Gly Leu Trp Asp Ser Ile Lys Ser Phe Thr Val
1205 1210 1215

Ser Leu His Lys Glu Asn Lys Lys Glu Lys Asp Val Leu Asn Ile
1220 1225 1230

Phe Ser Val Ala Ser Gly His Leu Tyr Glu Arg Phe Leu Arg Ile
1235 1240 1245

Met Met Leu Ser Val Leu Arg Asn Thr Lys Thr Pro Val Lys Phe
1250 1255 1260

Trp Leu Leu Lys Asn Tyr Leu Ser Pro Thr Phe Lys Glu Val Ile
1265 1270 1275

Pro His Met Ala Lys Glu Tyr Gly Phe Arg Tyr Glu Leu Val Gln
1280 1285 1290

Tyr Arg Trp Pro Arg Trp Leu Arg Gln Gln Thr Glu Arg Gln Arg
1295 1300 1305

Ile Ile Trp Gly Tyr Lys Ile Leu Phe Leu Asp Val Leu Phe Pro
1310 1315 1320

Leu Ala Val Asp Lys Ile Ile Phe Val Asp Ala Asp Gln Ile Val
1325 1330 1335

Arg His Asp Leu Lys Glu Leu Arg Asp Phe Asp Leu Asp Gly Ala
1340 1345 1350

Pro Tyr Gly Tyr Thr Pro Phe Cys Asp Ser Arg Arg Glu Met Asp
1355 1360 1365

Gly Tyr Arg Phe Trp Lys Thr Gly Tyr Trp Ala Ser His Leu Leu
1370 1375 1380

Arg Arg Lys Tyr His Ile Ser Ala Leu Tyr Val Val Asp Leu Lys
1385 1390 1395

Lys Phe Arg Arg Ile Gly Ala Gly Asp Arg Leu Arg Ser Gln Tyr
1400 1405 1410

Gln Ala Leu Ser Gln Asp Pro Asn Ser Leu Ser Asn Leu Asp Gln
1415 1420 1425

Asp Leu Pro Asn Asn Met Ile Tyr Gln Val Ala Ile Lys Ser Leu
1430 1435 1440

Pro Gln Asp Trp Leu Trp Cys Glu Thr Trp Cys Asp Asp Glu Ser
1445 1450 1455

Lys Gln Arg Ala Lys Thr Ile Asp Leu Cys Asn Asn Pro Lys Thr
1460 1465 1470

Lys Glu Ser Lys Leu Lys Ala Ala Ala Arg Ile Val Pro Glu Trp
1475 1480 1485

Val Glu Tyr Asp Ala Glu Ile Arg Gln Leu Leu Asp His Leu Glu
1490 1495 1500

Asn Lys Lys Gln Asp Thr Ile Leu Thr His Asp Glu Leu
1505 1510 1515

<210> 122
<211> 798
<212> PRT
<213> Homo sapiens

<400> 122

Met Asn Leu Gln Pro Ile Phe Trp Ile Gly Leu Ile Ser Ser Val Cys
1 5 10 15

Cys Val Phe Ala Gln Thr Asp Glu Asn Arg Cys Leu Lys Ala Asn Ala
20 25 30

Lys Ser Cys Gly Glu Cys Ile Gln Ala Gly Pro Asn Cys Gly Trp Cys
35 40 45

Thr Asn Ser Thr Phe Leu Gln Glu Gly Met Pro Thr Ser Ala Arg Cys
50 55 60

Asp Asp Leu Glu Ala Leu Lys Lys Lys Gly Cys Pro Pro Asp Asp Ile
65 70 75 80

Glu Asn Pro Arg Gly Ser Lys Asp Ile Lys Lys Asn Lys Asn Val Thr
85 90 95

Asn Arg Ser Lys Gly Thr Ala Glu Lys Leu Lys Pro Glu Asp Ile His
100 105 110

Gln Ile Gln Pro Gln Gln Leu Val Leu Arg Leu Arg Ser Gly Glu Pro
115 120 125

Gln Thr Phe Thr Leu Lys Phe Lys Arg Ala Glu Asp Tyr Pro Ile Asp
130 135 140

Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp Asp Leu Glu
145 150 155 160

Asn Val Lys Ser Leu Gly Thr Asp Leu Met Asn Glu Met Arg Arg Ile
165 170 175

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Thr Ser Asp Phe Arg Ile Gly Phe Gly Ser Phe Val Glu Lys Thr Val
            180                 185                 190

Met Pro Tyr Ile Ser Thr Thr Pro Ala Lys Leu Arg Asn Pro Cys Thr
        195                 200                 205

Ser Glu Gln Asn Cys Thr Thr Pro Phe Ser Tyr Lys Asn Val Leu Ser
    210                 215                 220

Leu Thr Asn Lys Gly Glu Val Phe Asn Glu Leu Val Gly Lys Gln Arg
225                 230                 235                 240

Ile Ser Gly Asn Leu Asp Ser Pro Glu Gly Gly Phe Asp Ala Ile Met
                245                 250                 255

Gln Val Ala Val Cys Gly Ser Leu Ile Gly Trp Arg Asn Val Thr Arg
            260                 265                 270

Leu Leu Val Phe Ser Thr Asp Ala Gly Phe His Phe Ala Gly Asp Gly
        275                 280                 285

Lys Leu Gly Gly Ile Val Leu Pro Asn Asp Gly Gln Cys His Leu Glu
    290                 295                 300

Asn Asn Met Tyr Thr Met Ser His Tyr Tyr Asp Tyr Pro Ser Ile Ala
305                 310                 315                 320

His Leu Val Gln Lys Leu Ser Glu Asn Asn Ile Gln Thr Ile Phe Ala
                325                 330                 335

Val Thr Glu Glu Phe Gln Pro Val Tyr Lys Glu Leu Lys Asn Leu Ile
            340                 345                 350

Pro Lys Ser Ala Val Gly Thr Leu Ser Ala Asn Ser Ser Asn Val Ile
        355                 360                 365

Gln Leu Ile Ile Asp Ala Tyr Asn Ser Leu Ser Ser Glu Val Ile Leu
    370                 375                 380

Glu Asn Gly Lys Leu Ser Glu Gly Val Thr Ile Ser Tyr Lys Ser Tyr
385                 390                 395                 400

Cys Lys Asn Gly Val Asn Gly Thr Gly Glu Asn Gly Arg Lys Cys Ser
                405                 410                 415

Asn Ile Ser Ile Gly Asp Glu Val Gln Phe Glu Ile Ser Ile Thr Ser
            420                 425                 430

Asn Lys Cys Pro Lys Lys Asp Ser Asp Ser Phe Lys Ile Arg Pro Leu
        435                 440                 445

Gly Phe Thr Glu Glu Val Glu Val Ile Leu Gln Tyr Ile Cys Glu Cys
    450                 455                 460

Glu Cys Gln Ser Glu Gly Ile Pro Glu Ser Pro Lys Cys His Glu Gly
465                 470                 475                 480

Asn Gly Thr Phe Glu Cys Gly Ala Cys Arg Cys Asn Glu Gly Arg Val
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                485                 490                 495

Gly Arg His Cys Glu Cys Ser Thr Asp Glu Val Asn Ser Glu Asp Met
            500                 505                 510

Asp Ala Tyr Cys Arg Lys Glu Asn Ser Ser Glu Ile Cys Ser Asn Asn
        515                 520                 525

Gly Glu Cys Val Cys Gly Gln Cys Val Cys Arg Lys Arg Asp Asn Thr
    530                 535                 540

Asn Glu Ile Tyr Ser Gly Lys Phe Cys Glu Cys Asp Asn Phe Asn Cys
545                 550                 555                 560

Asp Arg Ser Asn Gly Leu Ile Cys Gly Gly Asn Gly Val Cys Lys Cys
                565                 570                 575

Arg Val Cys Glu Cys Asn Pro Asn Tyr Thr Gly Ser Ala Cys Asp Cys
            580                 585                 590

Ser Leu Asp Thr Ser Thr Cys Glu Ala Ser Asn Gly Gln Ile Cys Asn
        595                 600                 605

Gly Arg Gly Ile Cys Glu Cys Gly Val Cys Lys Cys Thr Asp Pro Lys
    610                 615                 620

Phe Gln Gly Gln Thr Cys Glu Met Cys Gln Thr Cys Leu Gly Val Cys
625                 630                 635                 640

Ala Glu His Lys Glu Cys Val Gln Cys Arg Ala Phe Asn Lys Gly Glu
                645                 650                 655

Lys Lys Asp Thr Cys Thr Gln Glu Cys Ser Tyr Phe Asn Ile Thr Lys
            660                 665                 670

Val Glu Ser Arg Asp Lys Leu Pro Gln Pro Val Gln Pro Asp Pro Val
        675                 680                 685

Ser His Cys Lys Glu Lys Asp Val Asp Asp Cys Trp Phe Tyr Phe Thr
    690                 695                 700

Tyr Ser Val Asn Gly Asn Asn Glu Val Met Val His Val Val Glu Asn
705                 710                 715                 720

Pro Glu Cys Pro Thr Gly Pro Asp Ile Ile Pro Ile Val Ala Gly Val
                725                 730                 735

Val Ala Gly Ile Val Leu Ile Gly Leu Ala Leu Leu Leu Ile Trp Lys
            740                 745                 750

Leu Leu Met Ile Ile His Asp Arg Arg Glu Phe Ala Lys Phe Glu Lys
        755                 760                 765

Glu Lys Met Asn Ala Lys Trp Asp Thr Gly Glu Asn Pro Ile Tyr Lys
    770                 775                 780

Ser Ala Val Thr Thr Val Val Asn Pro Lys Tyr Glu Gly Lys
785                 790                 795
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<210> 123
<211> 317
<212> PRT
<213> Homo sapiens

<400> 123

Met Thr Glu Gln Met Thr Leu Arg Gly Thr Leu Lys Gly His Asn Gly
1 5 10 15

Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile Leu
20 25 30

Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys Leu Thr Arg Asp
35 40 45

Glu Thr Asn Tyr Gly Ile Pro Gln Arg Ala Leu Arg Gly His Ser His
50 55 60

Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln Phe Ala Leu Ser
65 70 75 80

Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp Leu Thr Thr Gly Thr
85 90 95

Thr Thr Arg Arg Phe Val Gly His Thr Lys Asp Val Leu Ser Val Ala
100 105 110

Phe Ser Ser Asp Asn Arg Gln Ile Val Ser Gly Ser Arg Asp Lys Thr
115 120 125

Ile Lys Leu Trp Asn Thr Leu Gly Val Cys Lys Tyr Thr Val Gln Asp
130 135 140

Glu Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser
145 150 155 160

Ser Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val
165 170 175

Trp Asn Leu Ala Asn Cys Lys Leu Lys Thr Asn His Ile Gly His Thr
180 185 190

Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala
195 200 205

Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly
210 215 220

Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys
225 230 235 240

Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
245 250 255

Lys Ile Trp Asp Leu Glu Gly Lys Ile Ile Val Asp Glu Leu Lys Gln
260 265 270

Glu Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser
275 280 285

Leu Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp
290 295 300

Asn Leu Val Arg Val Trp Gln Val Thr Ile Gly Thr Arg
305 310 315

<210> 124
<211> 351
<212> PRT
<213> Homo sapiens

<400> 124

Met Gln Arg Ala Leu Pro Gly Ala Arg Gln His Leu Gly Ala Ile Leu
1 5 10 15

Ala Ser Ala Ser Val Val Val Lys Ala Leu Cys Ala Ala Val Leu Phe
20 25 30

Leu Tyr Leu Leu Ser Phe Ala Val Asp Thr Gly Cys Leu Ala Val Thr
35 40 45

Pro Gly Tyr Leu Phe Pro Pro Asn Phe Trp Ile Trp Thr Leu Ala Thr
50 55 60

His Gly Leu Met Glu Gln His Val Trp Asp Val Ala Ile Ser Leu Thr
65 70 75 80

Thr Val Val Val Ala Gly Arg Leu Leu Glu Pro Leu Trp Gly Ala Leu
85 90 95

Glu Leu Leu Ile Phe Phe Ser Val Val Asn Val Ser Val Gly Leu Leu
100 105 110

Gly Ala Phe Ala Tyr Leu Leu Thr Tyr Met Ala Ser Phe Asn Leu Val
115 120 125

Tyr Leu Phe Thr Val Arg Ile His Gly Ala Leu Gly Phe Leu Gly Gly
130 135 140

Val Leu Val Ala Leu Lys Gln Thr Met Gly Asp Cys Val Val Leu Arg
145 150 155 160

Val Pro Gln Val Arg Val Ser Val Met Pro Met Leu Leu Leu Ala Leu
165 170 175

Leu Leu Leu Leu Arg Leu Ala Thr Leu Leu Gln Ser Pro Ala Leu Ala
180 185 190

Ser Tyr Gly Phe Gly Leu Leu Ser Ser Trp Val Tyr Leu Arg Phe Tyr
195 200 205

Gln Arg His Ser Arg Gly Arg Gly Asp Met Ala Asp His Phe Ala Phe
210 215 220

Ala Thr Phe Phe Pro Glu Ile Leu Gln Pro Val Val Gly Leu Leu Ala
225 230 235 240

Asn Leu Val His Ser Leu Leu Val Lys Val Lys Ile Cys Gln Lys Thr
245 250 255

Val Lys Arg Tyr Asp Val Gly Ala Pro Ser Ser Ile Thr Ile Ser Leu
260 265 270

Pro Gly Thr Asp Pro Gln Asp Ala Glu Arg Arg Arg Gln Leu Ala Leu
275 280 285

Lys Ala Leu Asn Glu Arg Leu Lys Arg Val Glu Asp Gln Ser Ile Trp
290 295 300

Pro Ser Met Asp Asp Asp Glu Glu Glu Ser Gly Ala Lys Val Asp Ser
305 310 315 320

Pro Leu Pro Ser Asp Lys Ala Pro Thr Pro Pro Gly Lys Gly Ala Ala
325 330 335

Pro Glu Ser Ser Leu Ile Thr Phe Glu Ala Ala Pro Pro Thr Leu
340 345 350

<210> 125
<211> 310
<212> PRT
<213> Homo sapiens

<400> 125

Met Arg Arg Ala Ala Leu Trp Leu Trp Leu Cys Ala Leu Ala Leu Ser
1 5 10 15

Leu Gln Leu Ala Leu Pro Gln Ile Val Ala Thr Asn Leu Pro Pro Glu
20 25 30

Asp Gln Asp Gly Ser Gly Asp Asp Ser Asp Asn Phe Ser Gly Ser Gly
35 40 45

Ala Gly Ala Leu Gln Asp Ile Thr Leu Ser Gln Gln Thr Pro Ser Thr
50 55 60

Trp Lys Asp Thr Gln Leu Leu Thr Ala Ile Pro Thr Ser Pro Glu Pro
65 70 75 80

Thr Gly Leu Glu Ala Thr Ala Ala Ser Thr Ser Thr Leu Pro Ala Gly
85 90 95

Glu Gly Pro Lys Glu Gly Glu Ala Val Val Leu Pro Glu Val Glu Pro
100 105 110

Gly Leu Thr Ala Arg Glu Gln Glu Ala Thr Pro Arg Pro Arg Glu Thr
115 120 125

Thr Gln Leu Pro Thr Thr His Gln Ala Ser Thr Thr Thr Ala Thr Thr
130 135 140

Ala Gln Glu Pro Ala Thr Ser His Pro His Arg Asp Met Gln Pro Gly
145 150 155 160

His His Glu Thr Ser Thr Pro Ala Gly Pro Ser Gln Ala Asp Leu His
165 170 175

Thr Pro His Thr Glu Asp Gly Gly Pro Ser Ala Thr Glu Arg Ala Ala
180 185 190

Glu Asp Gly Ala Ser Ser Gln Leu Pro Ala Ala Glu Gly Ser Gly Glu
195 200 205

Gln Asp Phe Thr Phe Glu Thr Ser Gly Glu Asn Thr Ala Val Val Ala
210 215 220

Val Glu Pro Asp Arg Arg Asn Gln Ser Pro Val Asp Gln Gly Ala Thr
225 230 235 240

Gly Ala Ser Gln Gly Leu Leu Asp Arg Lys Glu Val Leu Gly Gly Val
245 250 255

Ile Ala Gly Gly Leu Val Gly Leu Ile Phe Ala Val Cys Leu Val Gly
260 265 270

Phe Met Leu Tyr Arg Met Lys Lys Lys Asp Glu Gly Ser Tyr Ser Leu
275 280 285

Glu Glu Pro Lys Gln Ala Asn Gly Gly Ala Tyr Gln Lys Pro Thr Lys
290 295 300

Gln Glu Glu Phe Tyr Ala
305 310

<210> 126
<211> 2174
<212> PRT
<213> Homo sapiens

<400> 126

Met Ser Ala Ser Phe Val Pro Asn Gly Ala Ser Leu Glu Asp Cys His
1 5 10 15

Cys Asn Leu Phe Cys Leu Ala Asp Leu Thr Gly Ile Lys Trp Lys Lys
20 25 30

Tyr Val Trp Gln Gly Pro Thr Ser Ala Pro Ile Leu Phe Pro Val Thr
35 40 45

Glu Glu Asp Pro Ile Leu Ser Ser Phe Ser Arg Cys Leu Lys Ala Asp
50 55 60

Val Leu Gly Val Trp Arg Arg Asp Gln Arg Pro Gly Arg Arg Glu Leu
65 70 75 80

Trp Ile Phe Trp Trp Gly Glu Asp Pro Val Leu Leu Thr Leu Phe Thr
85 90 95

Met Thr Tyr Gln Lys Lys Lys Met Glu Cys Gly Arg Met Asp Phe Pro
100 105 110

Met Asn Ala Val Leu Cys Phe Ser Lys Ala Val His Asn Leu Leu Glu
115 120 125

Arg Cys Leu Met Asn Arg Asn Phe Val Arg Ile Gly Lys Trp Phe Val
130 135 140

Lys Pro Tyr Glu Lys Asp Glu Lys Pro Ile Asn Lys Ser Glu His Leu
145 150 155 160

Ser Cys Ser Phe Thr Phe Phe Leu His Gly Asp Ser Asn Val Cys Thr
165 170 175

Ser Val Glu Ile Asn Gln His Gln Pro Val Tyr Leu Leu Ser Glu Glu
180 185 190

His Ile Thr Leu Ala Gln Gln Ser Asn Ser Pro Phe Gln Val Ile Leu
195 200 205

Cys Pro Phe Gly Leu Asn Gly Thr Leu Thr Gly Gln Ala Phe Lys Met
210 215 220

Ser Asp Ser Ala Thr Lys Lys Leu Ile Gly Glu Trp Lys Gln Phe Tyr
225 230 235 240

Pro Ile Ser Cys Cys Leu Lys Glu Met Ser Glu Glu Lys Gln Glu Asp
245 250 255

Met Asp Trp Glu Asp Asp Ser Leu Ala Ala Val Glu Val Leu Val Ala
260 265 270

Gly Val Arg Met Ile Tyr Pro Ala Cys Phe Val Leu Val Pro Gln Ser
275 280 285

Asp Ile Pro Thr Pro Ser Pro Val Gly Ser Thr His Cys Ser Ser Ser
290 295 300

Cys Leu Gly Val His Gln Val Pro Ala Ser Thr Arg Asp Pro Ala Met
305 310 315 320

Ser Ser Val Thr Leu Thr Pro Pro Thr Ser Pro Glu Glu Val Gln Thr
325 330 335

Val Asp Pro Gln Ser Val Gln Lys Trp Val Lys Phe Ser Ser Val Ser
340 345 350

Asp Gly Phe Asn Ser Asp Ser Thr Ser His His Gly Gly Lys Ile Pro
355 360 365

Arg Lys Leu Ala Asn His Val Val Asp Arg Val Trp Gln Glu Cys Asn
370 375 380

Met Asn Arg Ala Gln Asn Lys Lys Lys Tyr Ser Ala Ser Ser Gly Gly
385 390 395 400

Leu Cys Glu Glu Ala Thr Ala Ala Lys Val Ala Ser Trp Asp Phe Val
405 410 415

Glu Ala Thr Gln Arg Thr Asn Cys Ser Cys Leu Arg His Lys Asn Leu
420 425 430

Lys Ser Arg Asn Ala Gly Gln Gln Gly Gln Ala Pro Ser Leu Gly Gln
435 440 445

Gln Gln Gln Ile Leu Pro Lys His Lys Thr Asn Glu Lys Gln Glu Lys
450 455 460

Ser Glu Glu Pro Gln Lys Arg Pro Leu Thr Pro Phe His His Arg Val
465 470 475 480

Ser Val Ser Asp Asp Val Gly Met Asp Ala Asp Ser Ala Ser Gln Arg
485 490 495

Leu Val Ile Ser Ala Pro Asp Ser Gln Val Arg Phe Ser Asn Ile Arg
500 505 510

Thr Asn Asp Val Ala Lys Thr Pro Gln Met His Gly Thr Glu Met Ala
515 520 525

Asn Ser Pro Gln Pro Pro Pro Leu Ser Pro His Pro Cys Asp Val Val
530 535 540

Asp Glu Gly Val Thr Lys Thr Pro Ser Thr Pro Gln Ser Gln His Phe
545 550 555 560

Tyr Gln Met Pro Thr Pro Asp Pro Leu Val Pro Ser Lys Pro Met Glu
565 570 575

Asp Arg Ile Asp Ser Leu Ser Gln Ser Phe Pro Pro Gln Tyr Gln Glu
580 585 590

Ala Val Glu Pro Thr Val Tyr Val Gly Thr Ala Val Asn Leu Glu Glu
595 600 605

Asp Glu Ala Asn Ile Ala Trp Lys Tyr Tyr Lys Phe Pro Lys Lys Lys
610 615 620

Asp Val Glu Phe Leu Pro Pro Gln Leu Pro Ser Asp Lys Phe Lys Asp
625 630 635 640

Asp Pro Val Gly Pro Phe Gly Gln Glu Ser Val Thr Ser Val Thr Glu
645 650 655

Leu Met Val Gln Cys Lys Lys Pro Leu Lys Val Ser Asp Glu Leu Val
660 665 670

Gln Gln Tyr Gln Ile Lys Asn Gln Cys Leu Ser Ala Ile Ala Ser Asp
675 680 685

Ala Glu Gln Glu Pro Lys Ile Asp Pro Tyr Ala Phe Val Glu Gly Asp
690 695 700

Glu Glu Phe Leu Phe Pro Asp Lys Lys Asp Arg Gln Asn Ser Glu Arg
705 710 715 720

Glu Ala Gly Lys Lys His Lys Val Glu Asp Gly Thr Ser Ser Val Thr
725 730 735

Val Leu Ser His Glu Glu Asp Ala Met Ser Leu Phe Ser Pro Ser Ile
740 745 750

Lys Gln Asp Ala Pro Arg Pro Thr Ser His Ala Arg Pro Pro Ser Thr
755 760 765

Ser Leu Ile Tyr Asp Ser Asp Leu Ala Val Ser Tyr Thr Asp Leu Asp
770 775 780

Asn Leu Phe Asn Ser Asp Glu Asp Glu Leu Thr Pro Gly Ser Lys Arg
785 790 795 800

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Ser Ala Asn Gly Ser Asp Asp Lys Ala Ser Cys Lys Glu Ser Lys Thr
                805                 810                 815

Gly Asn Leu Asp Pro Leu Ser Cys Ile Ser Thr Ala Asp Leu His Lys
            820                 825                 830

Met Tyr Pro Thr Pro Pro Ser Leu Glu Gln His Ile Met Gly Phe Ser
        835                 840                 845

Pro Met Asn Met Asn Asn Lys Glu Tyr Gly Ser Met Asp Thr Thr Pro
    850                 855                 860

Gly Gly Thr Val Leu Glu Gly Asn Ser Ser Ser Ile Gly Ala Gln Phe
865                 870                 875                 880

Lys Ile Glu Val Asp Glu Gly Phe Cys Ser Pro Lys Pro Ser Glu Ile
                885                 890                 895

Lys Asp Phe Ser Tyr Val Tyr Lys Pro Glu Asn Cys Gln Ile Leu Val
            900                 905                 910

Gly Cys Ser Met Phe Ala Pro Leu Lys Thr Leu Pro Ser Gln Tyr Leu
        915                 920                 925

Pro Leu Ile Lys Leu Pro Glu Glu Cys Ile Tyr Arg Gln Ser Trp Thr
    930                 935                 940

Val Gly Lys Leu Glu Leu Leu Ser Ser Gly Pro Ser Met Pro Phe Ile
945                 950                 955                 960

Lys Glu Gly Asp Gly Ser Asn Met Asp Gln Glu Tyr Gly Thr Ala Tyr
                965                 970                 975

Thr Pro Gln Thr His Thr Ser Cys Gly Met Pro Pro Ser Ser Ala Pro
            980                 985                 990

Pro Ser Asn Ser Gly Ala Gly Ile  Leu Pro Ser Pro Ser  Thr Pro Arg
        995                 1000                1005

Phe Pro  Thr Pro Arg Thr Pro  Arg Thr Pro Arg Thr  Pro Arg Gly
    1010                1015                1020

Ala Gly  Gly Pro Ala Ser Ala  Gln Gly Ser Val Lys  Tyr Glu Asn
    1025                1030                1035

Ser Asp  Leu Tyr Ser Pro Ala  Ser Thr Pro Ser Thr  Cys Arg Pro
    1040                1045                1050

Leu Asn  Ser Val Glu Pro Ala  Thr Val Pro Ser Ile  Pro Glu Ala
    1055                1060                1065

His Ser  Leu Tyr Val Asn Leu  Ile Leu Ser Glu Ser  Val Met Asn
    1070                1075                1080

Leu Phe  Lys Asp Cys Asn Ser  Asp Ser Cys Cys Ile  Cys Val Cys
    1085                1090                1095

Asn Met  Asn Ile Lys Gly Ala  Asp Val Gly Val Tyr  Ile Pro Asp
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    1100                1105                1110

Pro Thr  Gln Glu Ala Gln Tyr  Arg Cys Thr Cys Gly  Phe Ser Ala
    1115                1120                1125

Val Met  Asn Arg Lys Phe Gly  Asn Asn Ser Gly Leu  Phe Leu Glu
    1130                1135                1140

Asp Glu  Leu Asp Ile Ile Gly  Arg Asn Thr Asp Cys  Gly Lys Glu
    1145                1150                1155

Ala Glu  Lys Arg Phe Glu Ala  Leu Arg Ala Thr Ser  Ala Glu His
    1160                1165                1170

Val Asn  Gly Gly Leu Lys Glu  Ser Glu Lys Leu Ser  Asp Asp Leu
    1175                1180                1185

Ile Leu  Leu Leu Gln Asp Gln  Cys Thr Asn Leu Phe  Ser Pro Phe
    1190                1195                1200

Gly Ala  Ala Asp Gln Asp Pro  Phe Pro Lys Ser Gly  Val Ile Ser
    1205                1210                1215

Asn Trp  Val Arg Val Glu Glu  Arg Asp Cys Cys Asn  Asp Cys Tyr
    1220                1225                1230

Leu Ala  Leu Glu His Gly Arg  Gln Phe Met Asp Asn  Met Ser Gly
    1235                1240                1245

Gly Lys  Val Asp Glu Ala Leu  Val Lys Ser Ser Cys  Leu His Pro
    1250                1255                1260

Trp Ser  Lys Arg Asn Asp Val  Ser Met Gln Cys Ser  Gln Asp Ile
    1265                1270                1275

Leu Arg  Met Leu Leu Ser Leu  Gln Pro Val Leu Gln  Asp Ala Ile
    1280                1285                1290

Gln Lys  Lys Arg Thr Val Arg  Pro Trp Gly Val Gln  Gly Pro Leu
    1295                1300                1305

Thr Trp  Gln Gln Phe His Lys  Met Ala Gly Arg Gly  Ser Tyr Gly
    1310                1315                1320

Thr Asp  Glu Ser Pro Glu Pro  Leu Pro Ile Pro Thr  Phe Leu Leu
    1325                1330                1335

Gly Tyr  Asp Tyr Asp Tyr Leu  Val Leu Ser Pro Phe  Ala Leu Pro
    1340                1345                1350

Tyr Trp  Glu Arg Leu Met Leu  Glu Pro Tyr Gly Ser  Gln Arg Asp
    1355                1360                1365

Ile Ala  Tyr Val Val Leu Cys  Pro Glu Asn Glu Ala  Leu Leu Asn
    1370                1375                1380

Gly Ala  Lys Ser Phe Phe Arg  Asp Leu Thr Ala Ile  Tyr Glu Ser
    1385                1390                1395
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Cys Arg Leu Gly Gln His Arg Pro Val Ser Arg Leu Leu Thr Asp
1400 1405 1410

Gly Ile Met Arg Val Gly Ser Thr Ala Ser Lys Lys Leu Ser Glu
1415 1420 1425

Lys Leu Val Ala Glu Trp Phe Ser Gln Ala Ala Asp Gly Asn Asn
1430 1435 1440

Glu Ala Phe Ser Lys Leu Lys Leu Tyr Ala Gln Val Cys Arg Tyr
1445 1450 1455

Asp Leu Gly Pro Tyr Leu Ala Ser Leu Pro Leu Asp Ser Ser Leu
1460 1465 1470

Leu Ser Gln Pro Asn Leu Val Ala Pro Thr Ser Gln Ser Leu Ile
1475 1480 1485

Thr Pro Pro Gln Met Thr Asn Thr Gly Asn Ala Asn Thr Pro Ser
1490 1495 1500

Ala Thr Leu Ala Ser Ala Ala Ser Ser Thr Met Thr Val Thr Ser
1505 1510 1515

Gly Val Ala Ile Ser Thr Ser Val Ala Thr Ala Asn Ser Thr Leu
1520 1525 1530

Thr Thr Ala Ser Thr Ser Ser Ser Ser Ser Ser Asn Leu Asn Ser
1535 1540 1545

Gly Val Ser Ser Asn Lys Leu Pro Ser Phe Pro Pro Phe Gly Ser
1550 1555 1560

Met Asn Ser Asn Ala Ala Gly Ser Met Ser Thr Gln Ala Asn Thr
1565 1570 1575

Val Gln Ser Gly Gln Leu Gly Gly Gln Gln Thr Ser Ala Leu Gln
1580 1585 1590

Thr Ala Gly Ile Ser Gly Glu Ser Ser Ser Leu Pro Thr Gln Pro
1595 1600 1605

His Pro Asp Val Ser Glu Ser Thr Met Asp Arg Asp Lys Val Gly
1610 1615 1620

Ile Pro Thr Asp Gly Asp Ser His Ala Val Thr Tyr Pro Pro Ala
1625 1630 1635

Ile Val Val Tyr Ile Ile Asp Pro Phe Thr Tyr Glu Asn Thr Asp
1640 1645 1650

Glu Ser Thr Asn Ser Ser Ser Val Trp Thr Leu Gly Leu Leu Arg
1655 1660 1665

Cys Phe Leu Glu Met Val Gln Thr Leu Pro Pro His Ile Lys Ser
1670 1675 1680

Thr Val Ser Val Gln Ile Ile Pro Cys Gln Tyr Leu Leu Gln Pro
1685 1690 1695

Val Lys His Glu Asp Arg Glu Ile Tyr Pro Gln His Leu Lys Ser
1700 1705 1710

Leu Ala Phe Ser Ala Phe Thr Gln Cys Arg Arg Pro Leu Pro Thr
1715 1720 1725

Ser Thr Asn Val Lys Thr Leu Thr Gly Phe Gly Pro Gly Leu Ala
1730 1735 1740

Met Glu Thr Ala Leu Arg Ser Pro Asp Arg Pro Glu Cys Ile Arg
1745 1750 1755

Leu Tyr Ala Pro Pro Phe Ile Leu Ala Pro Val Lys Asp Lys Gln
1760 1765 1770

Thr Glu Leu Gly Glu Thr Phe Gly Glu Ala Gly Gln Lys Tyr Asn
1775 1780 1785

Val Leu Phe Val Gly Tyr Cys Leu Ser His Asp Gln Arg Trp Ile
1790 1795 1800

Leu Ala Ser Cys Thr Asp Leu Tyr Gly Glu Leu Leu Glu Thr Cys
1805 1810 1815

Ile Ile Asn Ile Asp Val Pro Asn Arg Ala Arg Arg Lys Lys Ser
1820 1825 1830

Ser Ala Arg Lys Phe Gly Leu Gln Lys Leu Trp Glu Trp Cys Leu
1835 1840 1845

Gly Leu Val Gln Met Ser Ser Leu Pro Trp Arg Val Val Ile Gly
1850 1855 1860

Arg Leu Gly Arg Ile Gly His Gly Glu Leu Lys Asp Trp Ser Cys
1865 1870 1875

Leu Leu Ser Arg Arg Asn Leu Gln Ser Leu Ser Lys Arg Leu Lys
1880 1885 1890

Asp Met Cys Arg Met Cys Gly Ile Ser Ala Ala Asp Ser Pro Ser
1895 1900 1905

Ile Leu Ser Ala Cys Leu Val Ala Met Glu Pro Gln Gly Ser Phe
1910 1915 1920

Val Ile Met Pro Asp Ser Val Ser Thr Gly Ser Val Phe Gly Arg
1925 1930 1935

Ser Thr Thr Leu Asn Met Gln Thr Ser Gln Leu Asn Thr Pro Gln
1940 1945 1950

Asp Thr Ser Cys Thr His Ile Leu Val Phe Pro Thr Ser Ala Ser
1955 1960 1965

Val Gln Val Ala Ser Ala Thr Tyr Thr Thr Glu Asn Leu Asp Leu
1970 1975 1980

Ala Phe Asn Pro Asn Asn Asp Gly Ala Asp Gly Met Gly Ile Phe
1985 1990 1995

Asp Leu Leu Asp Thr Gly Asp Asp Leu Asp Pro Asp Ile Ile Asn
2000 2005 2010

Ile Leu Pro Ala Ser Pro Thr Gly Ser Pro Val His Ser Pro Gly
2015 2020 2025

Ser His Tyr Pro His Gly Gly Asp Ala Gly Lys Gly Gln Ser Thr
2030 2035 2040

Asp Arg Leu Leu Ser Thr Glu Pro His Glu Glu Val Pro Asn Ile
2045 2050 2055

Leu Gln Gln Pro Leu Ala Leu Gly Tyr Phe Val Ser Thr Ala Lys
2060 2065 2070

Ala Gly Pro Leu Pro Asp Trp Phe Trp Ser Ala Cys Pro Gln Ala
2075 2080 2085

Gln Tyr Gln Cys Pro Leu Phe Leu Lys Ala Ser Leu His Leu His
2090 2095 2100

Val Pro Ser Val Gln Ser Asp Glu Leu Leu His Ser Lys His Ser
2105 2110 2115

His Pro Leu Asp Ser Asn Gln Thr Ser Asp Val Leu Arg Phe Val
2120 2125 2130

Leu Glu Gln Tyr Asn Ala Leu Ser Trp Leu Thr Cys Asp Pro Ala
2135 2140 2145

Thr Gln Asp Arg Arg Ser Cys Leu Pro Ile His Phe Val Val Leu
2150 2155 2160

Asn Gln Leu Tyr Asn Phe Ile Met Asn Met Leu
2165 2170

<210> 127
<211> 415
<212> PRT
<213> Homo sapiens

<400> 127

Met Glu Leu Arg Val Gly Asn Arg Tyr Arg Leu Gly Arg Lys Ile Gly
1 5 10 15

Ser Gly Ser Phe Gly Asp Ile Tyr Leu Gly Thr Asp Ile Ala Ala Gly
20 25 30

Glu Glu Val Ala Ile Lys Leu Glu Cys Val Lys Thr Lys His Pro Gln
35 40 45

Leu His Ile Glu Ser Lys Ile Tyr Lys Met Met Gln Gly Gly Val Gly
50 55 60

Ile Pro Thr Ile Arg Trp Cys Gly Ala Glu Gly Asp Tyr Asn Val Met
65 70 75 80

Val Met Glu Leu Leu Gly Pro Ser Leu Glu Asp Leu Phe Asn Phe Cys
85 90 95

Ser Arg Lys Phe Ser Leu Lys Thr Val Leu Leu Leu Ala Asp Gln Met
100 105 110

Ile Ser Arg Ile Glu Tyr Ile His Ser Lys Asn Phe Ile His Arg Asp
115 120 125

Val Lys Pro Asp Asn Phe Leu Met Gly Leu Gly Lys Lys Gly Asn Leu
130 135 140

Val Tyr Ile Ile Asp Phe Gly Leu Ala Lys Lys Tyr Arg Asp Ala Arg
145 150 155 160

Thr His Gln His Ile Pro Tyr Arg Glu Asn Lys Asn Leu Thr Gly Thr
165 170 175

Ala Arg Tyr Ala Ser Ile Asn Thr His Leu Gly Ile Glu Gln Ser Arg
180 185 190

Arg Asp Asp Leu Glu Ser Leu Gly Tyr Val Leu Met Tyr Phe Asn Leu
195 200 205

Gly Ser Leu Pro Trp Gln Gly Leu Lys Ala Ala Thr Lys Arg Gln Lys
210 215 220

Tyr Glu Arg Ile Ser Glu Lys Lys Met Ser Thr Pro Ile Glu Val Leu
225 230 235 240

Cys Lys Gly Tyr Pro Ser Glu Phe Ala Thr Tyr Leu Asn Phe Cys Arg
245 250 255

Ser Leu Arg Phe Asp Asp Lys Pro Asp Tyr Ser Tyr Leu Arg Gln Leu
260 265 270

Phe Arg Asn Leu Phe His Arg Gln Gly Phe Ser Tyr Asp Tyr Val Phe
275 280 285

Asp Trp Asn Met Leu Lys Phe Gly Ala Ser Arg Ala Ala Asp Asp Ala
290 295 300

Glu Arg Glu Arg Arg Asp Arg Glu Glu Arg Leu Arg His Ser Arg Asn
305 310 315 320

Pro Ala Thr Arg Gly Leu Pro Ser Thr Asp Ser Gly Arg Leu Arg Gly
325 330 335

Thr Gln Glu Val Ala Pro Pro Thr Pro Leu Thr Pro Thr Ser His Thr
340 345 350

Ala Asn Thr Ser Pro Arg Pro Val Ser Gly Met Glu Arg Glu Arg Lys
355 360 365

Val Ser Met Arg Leu His Arg Gly Ala Pro Val Asn Ile Ser Ser Ser
370 375 380

Asp Leu Thr Gly Arg Gln Asp Thr Ser Arg Met Ser Thr Ser Gln Ile
385 390 395 400

Pro Gly Arg Val Ala Ser Ser Gly Leu Gln Ser Val Val His Arg

405 410 415

<210> 128
<211> 204
<212> PRT
<213> Homo sapiens

<400> 128

Met Thr Glu Trp Glu Thr Ala Ala Pro Ala Val Ala Glu Thr Pro Asp
1 5 10 15

Ile Lys Leu Phe Gly Lys Trp Ser Thr Asp Asp Val Gln Ile Asn Asp
20 25 30

Ile Ser Leu Gln Asp Tyr Ile Ala Val Lys Glu Lys Tyr Ala Lys Tyr
35 40 45

Leu Pro His Ser Ala Gly Arg Tyr Ala Ala Asn Ala Phe Arg Lys Ala
50 55 60

Gln Cys Pro Ile Val Glu Arg Leu Thr Asn Ser Met Met Met His Gly
65 70 75 80

Arg Asn Asn Gly Lys Lys Leu Met Thr Val Arg Ile Val Lys His Ala
85 90 95

Phe Glu Ile Ile His Leu Leu Thr Gly Glu Asn Pro Leu Gln Val Leu
100 105 110

Val Asn Ala Ile Ile Asn Ser Gly Pro Arg Glu Asp Ser Thr Arg Ile
115 120 125

Gly Arg Ala Gly Thr Val Arg Arg Gln Ala Val Asp Val Ser Pro Leu
130 135 140

Arg Arg Val Asn Gln Ala Ile Trp Leu Leu Cys Thr Gly Ala Arg Glu
145 150 155 160

Ala Ala Phe Arg Asn Ile Lys Thr Ile Ala Glu Cys Leu Ala Asp Glu
165 170 175

Leu Ile Asn Ala Ala Lys Gly Ser Ser Asn Ser Tyr Ala Ile Lys Lys
180 185 190

Lys Asp Glu Leu Glu Arg Val Ala Lys Ser Asn Arg
195 200

<210> 129
<211> 694
<212> PRT
<213> Homo sapiens

<400> 129

Met Glu Asn Lys Ser Leu Glu Ser Ser Gln Thr Asp Leu Lys Leu Val
1 5 10 15

Ala His Pro Arg Ala Lys Ser Lys Val Trp Lys Tyr Phe Gly Phe Asp
20 25 30

Thr Asn Ala Glu Gly Cys Ile Leu Gln Trp Lys Lys Ile Tyr Cys Arg
35 40 45

Ile Cys Met Ala Gln Ile Ala Tyr Ser Gly Asn Thr Ser Asn Leu Ser
50 55 60

Tyr His Leu Glu Lys Asn His Pro Glu Glu Phe Cys Glu Phe Val Lys
65 70 75 80

Ser Asn Thr Glu Gln Met Arg Glu Ala Phe Ala Thr Ala Phe Ser Lys
85 90 95

Leu Lys Pro Glu Ser Ser Gln Gln Pro Gly Gln Asp Ala Leu Ala Val
100 105 110

Lys Ala Gly His Gly Tyr Asp Ser Lys Lys Gln Gln Glu Leu Thr Ala
115 120 125

Ala Val Leu Gly Leu Ile Cys Glu Gly Leu Tyr Pro Ala Ser Ile Val
130 135 140

Asp Glu Pro Thr Phe Lys Val Leu Leu Lys Thr Ala Asp Pro Arg Tyr
145 150 155 160

Glu Leu Pro Ser Arg Lys Tyr Ile Ser Thr Lys Ala Ile Pro Glu Lys
165 170 175

Tyr Gly Ala Val Arg Glu Val Ile Leu Lys Glu Leu Ala Glu Ala Thr
180 185 190

Trp Cys Gly Ile Ser Thr Asp Met Trp Arg Ser Glu Asn Gln Asn Arg
195 200 205

Ala Tyr Val Thr Leu Ala Ala His Phe Leu Gly Leu Gly Ala Pro Asn
210 215 220

Cys Leu Ser Met Gly Ser Arg Cys Leu Lys Thr Phe Glu Val Pro Glu
225 230 235 240

Glu Asn Thr Ala Glu Thr Ile Thr Arg Val Leu Tyr Glu Val Phe Ile
245 250 255

Glu Trp Gly Ile Ser Ala Lys Val Phe Gly Ala Thr Thr Asn Tyr Gly
260 265 270

Lys Asp Ile Val Lys Ala Cys Ser Leu Leu Asp Val Ala Val His Met
275 280 285

Pro Cys Leu Gly His Thr Phe Asn Ala Gly Ile Gln Gln Ala Phe Gln
290 295 300

Leu Pro Lys Leu Gly Ala Leu Leu Ser Arg Cys Arg Lys Leu Val Glu
305 310 315 320

Tyr Phe Gln Gln Ser Ala Val Ala Met Tyr Met Leu Tyr Glu Lys Gln
325 330 335

Lys Gln Gln Asn Val Ala His Cys Met Leu Val Ser Asn Arg Val Ser
340 345 350

Trp Trp Gly Ser Thr Leu Ala Met Leu Gln Arg Leu Lys Glu Gln Gln

```
        355                 360                 365

Phe Val Ile Ala Gly Val Leu Val Glu Asp Ser Asn Asn His His Leu
    370                 375                 380

Met Leu Glu Ala Ser Glu Trp Ala Thr Ile Glu Gly Leu Val Glu Leu
385                 390                 395                 400

Leu Gln Pro Phe Lys Gln Val Ala Glu Met Leu Ser Ala Ser Arg Tyr
                405                 410                 415

Pro Thr Ile Ser Met Val Lys Pro Leu Leu His Met Leu Leu Asn Thr
            420                 425                 430

Thr Leu Asn Ile Lys Glu Thr Asp Ser Lys Glu Leu Ser Met Ala Lys
        435                 440                 445

Glu Val Ile Ala Lys Glu Leu Ser Lys Thr Tyr Gln Glu Thr Pro Glu
    450                 455                 460

Ile Asp Met Phe Leu Asn Val Ala Thr Phe Leu Asp Pro Arg Tyr Lys
465                 470                 475                 480

Arg Leu Pro Phe Leu Ser Ala Phe Glu Arg Gln Gln Val Glu Asn Arg
                485                 490                 495

Val Val Glu Glu Ala Lys Gly Leu Leu Asp Lys Val Lys Asp Gly Gly
            500                 505                 510

Tyr Arg Pro Ala Glu Asp Lys Ile Phe Pro Val Pro Glu Glu Pro Pro
        515                 520                 525

Val Lys Lys Leu Met Arg Thr Ser Thr Pro Pro Pro Ala Ser Val Ile
    530                 535                 540

Asn Asn Met Leu Ala Glu Ile Phe Cys Gln Thr Gly Gly Val Glu Asp
545                 550                 555                 560

Gln Glu Glu Trp His Ala Gln Val Val Glu Glu Leu Ser Asn Phe Lys
                565                 570                 575

Ser Gln Lys Val Leu Gly Leu Asn Glu Asp Pro Leu Lys Trp Trp Ser
            580                 585                 590

Asp Arg Leu Ala Leu Phe Pro Leu Leu Pro Lys Val Leu Gln Lys Tyr
        595                 600                 605

Trp Cys Val Thr Ala Thr Arg Val Ala Pro Glu Arg Leu Phe Gly Ser
    610                 615                 620

Ala Ala Asn Val Val Ser Ala Lys Arg Asn Arg Leu Ala Pro Ala His
625                 630                 635                 640

Val Asp Glu Gln Val Phe Leu Tyr Glu Asn Ala Arg Ser Gly Ala Glu
                645                 650                 655

Ala Glu Pro Glu Asp Gln Asp Glu Gly Glu Trp Gly Leu Asp Gln Glu
            660                 665                 670
```



```
Gln Val Phe Ser Leu Gly Asp Gly Val Ser Gly Gly Phe Phe Gly Ile
        675                 680                 685

Arg Asp Ser Ser Phe Leu
    690
```

<210> 130
<211> 729
<212> PRT
<213> Homo sapiens

<400> 130

```
Met Gly Lys Lys Tyr Lys Asn Ile Val Leu Leu Lys Gly Leu Glu Val
1               5                   10                  15

Ile Asn Asp Tyr His Phe Arg Met Val Lys Ser Leu Leu Ser Asn Asp
            20                  25                  30

Leu Lys Leu Asn Leu Lys Met Arg Glu Glu Tyr Asp Lys Ile Gln Ile
        35                  40                  45

Ala Asp Leu Met Glu Glu Lys Phe Arg Gly Asp Ala Gly Leu Gly Lys
    50                  55                  60

Leu Ile Lys Ile Phe Glu Asp Ile Pro Thr Leu Glu Asp Leu Ala Glu
65                  70                  75                  80

Thr Leu Lys Lys Glu Lys Leu Lys Val Lys Gly Pro Ala Leu Ser Arg
                85                  90                  95

Lys Arg Lys Lys Glu Val His Ala Thr Ser Pro Ala Pro Ser Thr Ser
            100                 105                 110

Ser Thr Val Lys Thr Glu Gly Ala Glu Ala Thr Pro Gly Ala Gln Lys
        115                 120                 125

Arg Lys Lys Ser Thr Lys Glu Lys Ala Gly Pro Lys Gly Ser Lys Val
    130                 135                 140

Ser Glu Glu Gln Thr Gln Pro Pro Ser Pro Ala Gly Ala Gly Met Ser
145                 150                 155                 160

Thr Ala Met Gly Arg Ser Pro Ser Pro Lys Thr Ser Leu Ser Ala Pro
                165                 170                 175

Pro Asn Ser Ser Ser Thr Glu Asn Pro Lys Thr Val Ala Lys Cys Gln
            180                 185                 190

Val Thr Pro Arg Arg Asn Val Leu Gln Lys Arg Pro Val Ile Val Lys
        195                 200                 205

Val Leu Ser Thr Thr Lys Pro Phe Glu Tyr Glu Thr Pro Glu Met Glu
    210                 215                 220

Lys Lys Ile Met Phe His Ala Thr Val Ala Thr Gln Thr Gln Phe Phe
225                 230                 235                 240

His Val Lys Val Leu Asn Thr Ser Leu Lys Glu Lys Phe Asn Gly Lys
                245                 250                 255
```

```
Lys Ile Ile Ile Ile Ser Asp Tyr Leu Glu Tyr Asp Ser Leu Leu Glu
            260                 265                 270

Val Asn Glu Glu Ser Thr Val Ser Glu Ala Gly Pro Asn Gln Thr Phe
        275                 280                 285

Glu Val Pro Asn Lys Ile Ile Asn Arg Ala Lys Glu Thr Leu Lys Ile
    290                 295                 300

Asp Ile Leu His Lys Gln Ala Ser Gly Asn Ile Val Tyr Gly Val Phe
305                 310                 315                 320

Met Leu His Lys Lys Thr Val Asn Gln Lys Thr Thr Ile Tyr Glu Ile
                325                 330                 335

Gln Asp Asp Arg Gly Lys Met Asp Val Val Gly Thr Gly Gln Cys His
            340                 345                 350

Asn Ile Pro Cys Glu Glu Gly Asp Lys Leu Gln Leu Phe Cys Phe Arg
        355                 360                 365

Leu Arg Lys Lys Asn Gln Met Ser Lys Leu Ile Ser Glu Met His Ser
    370                 375                 380

Phe Ile Gln Ile Lys Lys Lys Thr Asn Pro Arg Asn Asn Asp Pro Lys
385                 390                 395                 400

Ser Met Lys Leu Pro Gln Glu Gln Arg Gln Leu Pro Tyr Pro Ser Glu
                405                 410                 415

Ala Ser Thr Thr Phe Pro Glu Ser His Leu Arg Thr Pro Gln Met Pro
            420                 425                 430

Pro Thr Thr Pro Ser Ser Ser Phe Phe Thr Lys Lys Ser Glu Asp Thr
        435                 440                 445

Ile Ser Lys Met Asn Asp Phe Met Arg Met Gln Ile Leu Lys Glu Gly
    450                 455                 460

Ser His Phe Pro Gly Pro Phe Met Thr Ser Ile Gly Pro Ala Glu Ser
465                 470                 475                 480

His Pro His Thr Pro Gln Met Pro Pro Ser Thr Pro Ser Ser Ser Phe
                485                 490                 495

Leu Thr Thr Leu Lys Pro Arg Leu Lys Thr Glu Pro Glu Glu Val Ser
            500                 505                 510

Ile Glu Asp Ser Ala Gln Ser Asp Leu Lys Glu Val Met Val Leu Asn
        515                 520                 525

Ala Thr Glu Ser Phe Val Tyr Glu Pro Lys Glu Gln Lys Lys Met Phe
    530                 535                 540

His Ala Thr Val Ala Thr Glu Asn Glu Val Phe Arg Val Lys Val Phe
545                 550                 555                 560

Asn Ile Asp Leu Lys Glu Lys Phe Thr Pro Lys Lys Ile Ile Ala Ile
                565                 570                 575
```



```
Ala Asn Tyr Val Cys Arg Asn Gly Phe Leu Glu Val Tyr Pro Phe Thr
            580                 585                 590

Leu Val Ala Asp Val Asn Ala Asp Arg Asn Met Glu Ile Pro Lys Gly
        595                 600                 605

Leu Ile Arg Ser Ala Ser Val Thr Pro Lys Ile Asn Gln Leu Cys Ser
    610                 615                 620

Gln Thr Lys Gly Ser Phe Val Asn Gly Val Phe Glu Val His Lys Lys
625                 630                 635                 640

Asn Val Arg Gly Glu Phe Thr Tyr Tyr Glu Ile Gln Asp Asn Thr Gly
                645                 650                 655

Lys Met Glu Val Val Val His Gly Arg Leu Asn Thr Ile Asn Cys Glu
            660                 665                 670

Glu Gly Asp Lys Leu Lys Leu Thr Ser Phe Glu Leu Ala Pro Lys Ser
        675                 680                 685

Gly Asn Thr Gly Glu Leu Arg Ser Val Ile His Ser His Ile Lys Val
    690                 695                 700

Ile Lys Thr Arg Lys Asn Lys Lys Asp Ile Leu Asn Pro Asp Ser Ser
705                 710                 715                 720

Met Glu Thr Ser Pro Asp Phe Phe Phe
                725
```

<210> 131
<211> 216
<212> PRT
<213> Homo sapiens

<400> 131

```
Met Leu Arg Leu Ser Glu Arg Asn Met Lys Val Leu Leu Ala Ala Ala
1               5                   10                  15

Leu Ile Ala Gly Ser Val Phe Phe Leu Leu Leu Pro Gly Pro Ser Ala
            20                  25                  30

Ala Asp Glu Lys Lys Lys Gly Pro Lys Val Thr Val Lys Val Tyr Phe
        35                  40                  45

Asp Leu Arg Ile Gly Asp Glu Asp Val Gly Arg Val Ile Phe Gly Leu
    50                  55                  60

Phe Gly Lys Thr Val Pro Lys Thr Val Asp Asn Phe Val Ala Leu Ala
65                  70                  75                  80

Thr Gly Glu Lys Gly Phe Gly Tyr Lys Asn Ser Lys Phe His Arg Val
                85                  90                  95

Ile Lys Asp Phe Met Ile Gln Gly Gly Asp Phe Thr Arg Gly Asp Gly
            100                 105                 110

Thr Gly Gly Lys Ser Ile Tyr Gly Glu Arg Phe Pro Asp Glu Asn Phe
        115                 120                 125
```

```
Lys Leu Lys His Tyr Gly Pro Gly Trp Val Ser Met Ala Asn Ala Gly
    130                 135                 140

Lys Asp Thr Asn Gly Ser Gln Phe Phe Ile Thr Thr Val Lys Thr Ala
145                 150                 155                 160

Trp Leu Asp Gly Lys His Val Val Phe Gly Lys Val Leu Glu Gly Met
                165                 170                 175

Glu Val Val Arg Lys Val Glu Ser Thr Lys Thr Asp Ser Arg Asp Lys
            180                 185                 190

Pro Leu Lys Asp Val Ile Ile Ala Asp Cys Gly Lys Ile Glu Val Glu
        195                 200                 205

Lys Pro Phe Ala Ile Ala Lys Glu
    210                 215
```

<210> 132
<211> 208
<212> PRT
<213> Homo sapiens

<400> 132

```
Met Lys Leu Leu Pro Ser Val Val Leu Lys Leu Phe Leu Ala Ala Val
1               5                   10                  15

Leu Ser Ala Leu Val Thr Gly Glu Ser Leu Glu Arg Leu Arg Arg Gly
            20                  25                  30

Leu Ala Ala Gly Thr Ser Asn Pro Asp Pro Pro Thr Val Ser Thr Asp
        35                  40                  45

Gln Leu Leu Pro Leu Gly Gly Gly Arg Asp Arg Lys Val Arg Asp Leu
    50                  55                  60

Gln Glu Ala Asp Leu Asp Leu Leu Arg Val Thr Leu Ser Ser Lys Pro
65                  70                  75                  80

Gln Ala Leu Ala Thr Pro Asn Lys Glu Glu His Gly Lys Arg Lys Lys
                85                  90                  95

Lys Gly Lys Gly Leu Gly Lys Lys Arg Asp Pro Cys Leu Arg Lys Tyr
            100                 105                 110

Lys Asp Phe Cys Ile His Gly Glu Cys Lys Tyr Val Lys Glu Leu Arg
        115                 120                 125

Ala Pro Ser Cys Ile Cys His Pro Gly Tyr His Gly Glu Arg Cys His
    130                 135                 140

Gly Leu Ser Leu Pro Val Glu Asn Arg Leu Tyr Thr Tyr Asp His Thr
145                 150                 155                 160

Thr Ile Leu Ala Val Val Ala Val Val Leu Ser Ser Val Cys Leu Leu
                165                 170                 175

Val Ile Val Gly Leu Leu Met Phe Arg Tyr His Arg Arg Gly Gly Tyr
            180                 185                 190
```



```
Asp Val Glu Asn Glu Glu Lys Val Lys Leu Gly Met Thr Asn Ser His
        195                 200                 205
```

<210> 133
<211> 178
<212> PRT
<213> Homo sapiens

<400> 133

```
Met Thr Thr Leu Arg Ala Phe Thr Cys Asp Asp Leu Phe Arg Phe Asn
1               5                   10                  15

Asn Ile Asn Leu Asp Pro Leu Thr Glu Thr Tyr Gly Ile Pro Phe Tyr
            20                  25                  30

Leu Gln Tyr Leu Ala His Trp Pro Glu Tyr Phe Ile Val Ala Glu Ala
        35                  40                  45

Pro Gly Gly Glu Leu Met Gly Tyr Ile Met Gly Lys Ala Glu Gly Ser
    50                  55                  60

Val Ala Arg Glu Glu Trp His Gly His Val Thr Ala Leu Ser Val Ala
65                  70                  75                  80

Pro Glu Phe Arg Arg Leu Gly Leu Ala Ala Lys Leu Met Glu Leu Leu
                85                  90                  95

Glu Glu Ile Ser Glu Arg Lys Gly Gly Phe Phe Val Asp Leu Phe Val
            100                 105                 110

Arg Val Ser Asn Gln Val Ala Val Asn Met Tyr Lys Gln Leu Gly Tyr
        115                 120                 125

Ser Val Tyr Arg Thr Val Ile Glu Tyr Tyr Ser Ala Ser Asn Gly Glu
    130                 135                 140

Pro Asp Glu Asp Ala Tyr Asp Met Arg Lys Ala Leu Ser Arg Asp Thr
145                 150                 155                 160

Glu Lys Lys Ser Ile Ile Pro Leu Pro His Pro Val Arg Pro Glu Asp
                165                 170                 175

Ile Glu
```

<210> 134
<211> 185
<212> PRT
<213> Homo sapiens

<400> 134

```
Met Gly Pro Glu Arg His Leu Ser Gly Ala Pro Ala Arg Met Ala Thr
1               5                   10                  15

Val Val Leu Gly Gly Asp Thr Met Gly Pro Glu Arg Ile Phe Pro Asn
            20                  25                  30

Gln Thr Glu Glu Leu Gly His Gln Gly Pro Ser Glu Gly Thr Gly Asp
        35                  40                  45
```

```
Trp Ser Ser Glu Glu Pro Glu Glu Glu Gln Glu Glu Thr Gly Ser Gly
 50                  55                  60

Pro Ala Gly Tyr Ser Tyr Gln Pro Leu Asn Gln Asp Pro Glu Gln Glu
65                  70                  75                  80

Glu Val Glu Leu Ala Pro Val Gly Asp Gly Asp Val Val Ala Asp Ile
                85                  90                  95

Gln Asp Arg Ile Gln Ala Leu Gly Leu His Leu Pro Asp Pro Pro Leu
            100                 105                 110

Glu Ser Glu Asp Glu Asp Glu Glu Gly Ala Thr Ala Leu Asn Asn His
        115                 120                 125

Ser Ser Ile Pro Met Asp Pro Glu His Val Glu Leu Val Lys Arg Thr
    130                 135                 140

Met Ala Gly Val Ser Leu Pro Ala Pro Gly Val Pro Ala Trp Ala Arg
145                 150                 155                 160

Glu Ile Ser Asp Ala Gln Trp Glu Asp Val Val Gln Lys Ala Leu Gln
                165                 170                 175

Ala Arg Gln Ala Ser Pro Ala Trp Lys
            180                 185
```

<210> 135
<211> 397
<212> PRT
<213> Homo sapiens

<400> 135

```
Met Asn Ala Gly Ser Asp Pro Val Val Ile Val Ser Ala Ala Arg Thr
1               5                   10                  15

Ile Ile Gly Ser Phe Asn Gly Ala Leu Ala Ala Val Pro Val Gln Asp
            20                  25                  30

Leu Gly Ser Thr Val Ile Lys Glu Val Leu Lys Arg Ala Thr Val Ala
        35                  40                  45

Pro Glu Asp Val Ser Glu Val Ile Phe Gly His Val Leu Ala Ala Gly
    50                  55                  60

Cys Gly Gln Asn Pro Val Arg Gln Ala Ser Val Gly Ala Gly Ile Pro
65                  70                  75                  80

Tyr Ser Val Pro Ala Trp Ser Cys Gln Met Ile Cys Gly Ser Gly Leu
                85                  90                  95

Lys Ala Val Cys Leu Ala Val Gln Ser Ile Gly Ile Gly Asp Ser Ser
            100                 105                 110

Ile Val Val Ala Gly Gly Met Glu Asn Met Ser Lys Ala Pro His Leu
        115                 120                 125

Ala Tyr Leu Arg Thr Gly Val Lys Ile Gly Glu Met Pro Leu Thr Asp
    130                 135                 140
```



```
Ser Ile Leu Cys Asp Gly Leu Thr Asp Ala Phe His Asn Cys His Met
145                 150                 155                 160

Gly Ile Thr Ala Glu Asn Val Ala Thr Lys Trp Gln Val Ser Arg Glu
                165                 170                 175

Asp Gln Asp Lys Val Ala Val Leu Ser Gln Asn Arg Thr Glu Asn Ala
            180                 185                 190

Gln Lys Ala Gly His Phe Asp Lys Glu Ile Val Pro Val Leu Val Ser
        195                 200                 205

Thr Arg Lys Gly Leu Ile Glu Val Lys Thr Asp Glu Phe Pro Arg His
    210                 215                 220

Gly Ser Asn Ile Glu Ala Met Ser Lys Leu Lys Pro Tyr Phe Leu Thr
225                 230                 235                 240

Asp Gly Thr Gly Thr Val Thr Pro Ala Asn Ala Ser Gly Ile Asn Asp
                245                 250                 255

Gly Ala Ala Ala Val Ala Leu Met Lys Lys Ser Glu Ala Asp Lys Arg
            260                 265                 270

Gly Leu Thr Pro Leu Ala Arg Ile Val Ser Trp Ser Gln Val Gly Val
        275                 280                 285

Glu Pro Ser Ile Met Gly Ile Gly Pro Ile Pro Ala Ile Lys Gln Ala
    290                 295                 300

Val Thr Lys Ala Gly Trp Ser Leu Glu Asp Val Asp Ile Phe Glu Ile
305                 310                 315                 320

Asn Glu Ala Phe Ala Ala Val Ser Ala Ala Ile Val Lys Glu Leu Gly
                325                 330                 335

Leu Asn Pro Glu Lys Val Asn Ile Glu Gly Gly Ala Ile Ala Leu Gly
            340                 345                 350

His Pro Leu Gly Ala Ser Gly Cys Arg Ile Leu Val Thr Leu Leu His
        355                 360                 365

Thr Leu Glu Arg Met Gly Arg Ser Arg Gly Val Ala Ala Leu Cys Ile
    370                 375                 380

Gly Gly Gly Met Gly Ile Ala Met Cys Val Gln Arg Glu
385                 390                 395
```

<210> 136
<211> 556
<212> PRT
<213> Homo sapiens

<400> 136

```
Met Glu Gly Pro Leu Ser Val Phe Gly Asp Arg Ser Thr Gly Glu Thr
1               5                   10                  15

Ile Arg Ser Gln Asn Val Met Ala Ala Ala Ser Ile Ala Asn Ile Val
            20                  25                  30
```

```
Lys Ser Ser Leu Gly Pro Val Gly Leu Asp Lys Met Leu Val Asp Asp
        35                  40                  45

Ile Gly Asp Val Thr Ile Thr Asn Asp Gly Ala Thr Ile Leu Lys Leu
    50                  55                  60

Leu Glu Val Glu His Pro Ala Ala Lys Val Leu Cys Glu Leu Ala Asp
65                  70                  75                  80

Leu Gln Asp Lys Glu Val Gly Asp Gly Thr Thr Ser Val Val Ile Ile
                85                  90                  95

Ala Ala Glu Leu Leu Lys Asn Ala Asp Glu Leu Val Lys Gln Lys Ile
            100                 105                 110

His Pro Thr Ser Val Ile Ser Gly Tyr Arg Leu Ala Cys Lys Glu Ala
        115                 120                 125

Val Arg Tyr Ile Asn Glu Asn Leu Ile Val Asn Thr Asp Glu Leu Gly
    130                 135                 140

Arg Asp Cys Leu Ile Asn Ala Ala Lys Thr Ser Met Ser Ser Lys Ile
145                 150                 155                 160

Ile Gly Ile Asn Gly Asp Phe Phe Ala Asn Met Val Val Asp Ala Val
                165                 170                 175

Leu Ala Ile Lys Tyr Thr Asp Ile Arg Gly Gln Pro Arg Tyr Pro Val
            180                 185                 190

Asn Ser Val Asn Ile Leu Lys Ala His Gly Arg Ser Gln Met Glu Ser
        195                 200                 205

Met Leu Ile Ser Gly Tyr Ala Leu Asn Cys Val Val Gly Ser Gln Gly
    210                 215                 220

Met Pro Lys Arg Ile Val Asn Ala Lys Ile Ala Cys Leu Asp Phe Ser
225                 230                 235                 240

Leu Gln Lys Thr Lys Met Lys Leu Gly Val Gln Val Val Ile Thr Asp
                245                 250                 255

Pro Glu Lys Leu Asp Gln Ile Arg Gln Arg Glu Ser Asp Ile Thr Lys
            260                 265                 270

Glu Arg Ile Gln Lys Ile Leu Ala Thr Gly Ala Asn Val Ile Leu Thr
        275                 280                 285

Thr Gly Gly Ile Asp Asp Met Cys Leu Lys Tyr Phe Val Glu Ala Gly
    290                 295                 300

Ala Met Ala Val Arg Arg Val Leu Lys Arg Asp Leu Lys Arg Ile Ala
305                 310                 315                 320

Lys Ala Ser Gly Ala Thr Ile Leu Ser Thr Leu Ala Asn Leu Glu Gly
                325                 330                 335

Glu Glu Thr Phe Glu Ala Ala Met Leu Gly Gln Ala Glu Glu Val Val
            340                 345                 350
```



```
Gln Glu Arg Ile Cys Asp Asp Glu Leu Ile Leu Ile Lys Asn Thr Lys
        355                 360                 365

Ala Arg Thr Ser Ala Ser Ile Ile Leu Arg Gly Ala Asn Asp Phe Met
    370                 375                 380

Cys Asp Glu Met Glu Arg Ser Leu His Asp Ala Leu Cys Val Val Lys
385                 390                 395                 400

Arg Val Leu Glu Ser Lys Ser Val Val Pro Gly Gly Gly Ala Val Glu
                405                 410                 415

Ala Ala Leu Ser Ile Tyr Leu Glu Asn Tyr Ala Thr Ser Met Gly Ser
            420                 425                 430

Arg Glu Gln Leu Ala Ile Ala Glu Phe Ala Arg Ser Leu Leu Val Ile
        435                 440                 445

Pro Asn Thr Leu Ala Val Asn Ala Ala Gln Asp Ser Thr Asp Leu Val
    450                 455                 460

Ala Lys Leu Arg Ala Phe His Asn Glu Ala Gln Val Asn Pro Glu Arg
465                 470                 475                 480

Lys Asn Leu Lys Trp Ile Gly Leu Asp Leu Ser Asn Gly Lys Pro Arg
                485                 490                 495

Asp Asn Lys Gln Ala Gly Val Phe Glu Pro Thr Ile Val Lys Val Lys
            500                 505                 510

Ser Leu Lys Phe Ala Thr Glu Ala Ala Ile Thr Ile Leu Arg Ile Asp
        515                 520                 525

Asp Leu Ile Lys Leu His Pro Glu Ile Leu Arg Ile Lys His Gly Ser
    530                 535                 540

Tyr Glu Asp Ala Val His Ser Gly Ala Leu Asn Asp
545                 550                 555
```

<210> 137
<211> 266
<212> PRT
<213> Homo sapiens

<400> 137

```
Met Pro Lys Gly Lys Lys Ala Lys Gly Lys Lys Val Ala Pro Ala Pro
1               5                   10                  15

Ala Val Val Lys Lys Gln Glu Ala Lys Lys Val Val Asn Pro Leu Phe
            20                  25                  30

Glu Lys Arg Pro Lys Asn Phe Gly Ile Gly Gln Asp Ile Gln Pro Lys
        35                  40                  45

Arg Asp Leu Thr Arg Phe Val Lys Trp Pro Arg Tyr Ile Arg Leu Gln
    50                  55                  60

Arg Gln Arg Ala Ile Leu Tyr Lys Arg Leu Lys Val Pro Pro Ala Ile
65                  70                  75                  80
```

```
Asn Gln Phe Thr Gln Ala Leu Asp Arg Gln Thr Ala Thr Gln Leu Leu
                85                  90                  95

Lys Leu Ala His Lys Tyr Arg Pro Glu Thr Lys Gln Glu Lys Lys Gln
            100                 105                 110

Arg Leu Leu Ala Arg Ala Glu Lys Lys Ala Ala Gly Lys Gly Asp Val
        115                 120                 125

Pro Thr Lys Arg Pro Pro Val Leu Arg Ala Gly Val Asn Thr Val Thr
    130                 135                 140

Thr Leu Val Glu Asn Lys Lys Ala Gln Leu Val Val Ile Ala His Asp
145                 150                 155                 160

Val Asp Pro Ile Glu Leu Val Val Phe Leu Pro Ala Leu Cys Arg Lys
                165                 170                 175

Met Gly Val Pro Tyr Cys Ile Ile Lys Gly Lys Ala Arg Leu Gly Arg
            180                 185                 190

Leu Val His Arg Lys Thr Cys Thr Thr Val Ala Phe Thr Gln Val Asn
        195                 200                 205

Ser Glu Asp Lys Gly Ala Leu Ala Lys Leu Val Glu Ala Ile Arg Thr
    210                 215                 220

Asn Tyr Asn Asp Arg Tyr Asp Glu Ile Arg Arg His Trp Gly Gly Asn
225                 230                 235                 240

Val Leu Gly Pro Lys Ser Val Ala Arg Ile Ala Lys Leu Glu Lys Ala
                245                 250                 255

Lys Ala Lys Glu Leu Ala Thr Lys Leu Gly
            260                 265
```

<210> 138
<211> 160
<212> PRT
<213> Homo sapiens

<400> 138

```
Met Asp Cys Gln Asn Gly His Gln His Ile Ser Gln Glu Leu Glu Val
1               5                   10                  15

Leu Arg Ile His Met Gln Leu Val Thr Val Gln Phe Thr Gln Leu Gly
            20                  25                  30

Lys Gly Ala Leu Glu Ile Ile Gln Val Leu Cys Gly Ile Ser Gln Gly
        35                  40                  45

Ser Gln His Leu Leu Ala Met Cys Leu Asp Phe Gly Val Ala His Asp
    50                  55                  60

Gly Arg Gly Arg Gly Gln Val Ala Lys Ala Val Lys Glu Pro Leu Gly
65                  70                  75                  80

Pro Trp Val Asp Asn Gln Glu Pro Ser Gln Gly Phe Ser Ser Ser Ile
                85                  90                  95
```



```
Phe His Ile His Leu Ala Pro Gln Ala Cys Asp Ser Ser Leu Val Leu
            100                 105                 110

Leu Cys Glu Met Thr His Gly Val Trp Thr Arg Ser Leu Leu Ile Thr
        115                 120                 125

Ser Asp Val Pro Glu Ala Ser Val Thr Gln Ile Leu Leu Cys Ala Met
    130                 135                 140

Trp Thr Leu Pro Ser His Ala Thr Thr Arg Glu Leu Thr Gln Trp Val
145                 150                 155                 160
```

<210> 139
<211> 172
<212> PRT
<213> Homo sapiens

<400> 139

```
Met Ile Ile Tyr Arg Asp Leu Ile Ser His Asp Glu Met Phe Ser Asp
1               5                   10                  15

Ile Tyr Lys Ile Arg Glu Ile Ala Asp Gly Leu Cys Leu Glu Val Glu
            20                  25                  30

Gly Lys Met Val Ser Arg Thr Glu Gly Asn Ile Asp Asp Ser Leu Ile
        35                  40                  45

Gly Gly Asn Ala Ser Ala Glu Gly Pro Glu Gly Glu Gly Thr Glu Ser
    50                  55                  60

Thr Val Ile Thr Gly Val Asp Ile Val Met Asn His His Leu Gln Glu
65                  70                  75                  80

Thr Ser Phe Thr Lys Glu Ala Tyr Lys Lys Tyr Ile Lys Asp Tyr Met
                85                  90                  95

Lys Ser Ile Lys Gly Lys Leu Glu Glu Gln Arg Pro Glu Arg Val Lys
            100                 105                 110

Pro Phe Met Thr Gly Ala Ala Glu Gln Ile Lys His Ile Leu Ala Asn
        115                 120                 125

Phe Lys Asn Tyr Gln Phe Phe Ile Gly Glu Asn Met Asn Pro Asp Gly
    130                 135                 140

Met Val Ala Leu Leu Asp Tyr Arg Glu Asp Gly Val Thr Pro Tyr Met
145                 150                 155                 160

Ile Phe Phe Lys Asp Gly Leu Glu Met Glu Lys Cys
                165                 170
```

<210> 140
<211> 133
<212> PRT
<213> Homo sapiens

<400> 140

```
Met Asn Asp Thr Val Thr Ile Arg Thr Arg Lys Phe Met Thr Asn Arg
1               5                   10                  15
```

```
Leu Leu Gln Arg Lys Gln Met Val Ile Asp Val Leu His Pro Gly Lys
            20                  25                  30

Ala Thr Val Pro Lys Thr Glu Ile Arg Glu Lys Leu Ala Lys Met Tyr
        35                  40                  45

Lys Thr Thr Pro Asp Val Ile Phe Val Phe Gly Phe Arg Thr His Phe
    50                  55                  60

Gly Gly Gly Lys Thr Thr Gly Phe Gly Met Ile Tyr Asp Ser Leu Asp
65                  70                  75                  80

Tyr Ala Lys Lys Asn Glu Pro Lys His Arg Leu Ala Arg His Gly Leu
                85                  90                  95

Tyr Glu Lys Lys Lys Thr Ser Arg Lys Gln Arg Lys Glu Arg Lys Asn
            100                 105                 110

Arg Met Lys Lys Val Arg Gly Thr Ala Lys Ala Asn Val Gly Ala Gly
        115                 120                 125

Lys Lys Pro Lys Glu
    130
```

<210> 141
<211> 604
<212> PRT
<213> Homo sapiens

<400> 141

```
Met Asn Ile Val Glu Asn Ser Ile Phe Leu Ser Asn Leu Met Lys Ser
1               5                   10                  15

Ala Tyr Thr Phe Glu Leu Lys Tyr Asp Leu Ser Cys Glu Leu Tyr Arg
            20                  25                  30

Met Ser Thr Tyr Ser Thr Phe Pro Ala Gly Val Pro Val Ser Glu Arg
        35                  40                  45

Ser Leu Ala Arg Ala Gly Phe Tyr Tyr Thr Gly Val Asn Asp Lys Val
    50                  55                  60

Lys Cys Phe Cys Cys Gly Leu Met Leu Asp Asn Trp Lys Arg Gly Asp
65                  70                  75                  80

Ser Pro Thr Glu Lys His Lys Lys Leu Tyr Pro Ser Cys Arg Phe Val
                85                  90                  95

Gln Ser Leu Asn Ser Val Asn Asn Leu Glu Ala Thr Ser Gln Pro Thr
            100                 105                 110

Phe Pro Ser Ser Val Thr Asn Ser Thr His Ser Leu Leu Pro Gly Thr
        115                 120                 125

Glu Asn Ser Gly Tyr Phe Arg Gly Ser Tyr Ser Asn Ser Pro Ser Asn
    130                 135                 140

Pro Val Asn Ser Arg Ala Asn Gln Asp Phe Ser Ala Leu Met Arg Ser
145                 150                 155                 160
```



```
Ser Tyr His Cys Ala Met Asn Asn Glu Asn Ala Arg Leu Leu Thr Phe
                165                 170                 175

Gln Thr Trp Pro Leu Thr Phe Leu Ser Pro Thr Asp Leu Ala Lys Ala
            180                 185                 190

Gly Phe Tyr Tyr Ile Gly Pro Gly Asp Arg Val Ala Cys Phe Ala Cys
        195                 200                 205

Gly Gly Lys Leu Ser Asn Trp Glu Pro Lys Asp Asn Ala Met Ser Glu
    210                 215                 220

His Leu Arg His Phe Pro Lys Cys Pro Phe Ile Glu Asn Gln Leu Gln
225                 230                 235                 240

Asp Thr Ser Arg Tyr Thr Val Ser Asn Leu Ser Met Gln Thr His Ala
                245                 250                 255

Ala Arg Phe Lys Thr Phe Phe Asn Trp Pro Ser Ser Val Leu Val Asn
            260                 265                 270

Pro Glu Gln Leu Ala Ser Ala Gly Phe Tyr Tyr Val Gly Asn Ser Asp
        275                 280                 285

Asp Val Lys Cys Phe Cys Cys Asp Gly Gly Leu Arg Cys Trp Glu Ser
    290                 295                 300

Gly Asp Asp Pro Trp Val Gln His Ala Lys Trp Phe Pro Arg Cys Glu
305                 310                 315                 320

Tyr Leu Ile Arg Ile Lys Gly Gln Glu Phe Ile Arg Gln Val Gln Ala
                325                 330                 335

Ser Tyr Pro His Leu Leu Glu Gln Leu Leu Ser Thr Ser Asp Ser Pro
            340                 345                 350

Gly Asp Glu Asn Ala Glu Ser Ser Ile Ile His Phe Glu Pro Gly Glu
        355                 360                 365

Asp His Ser Glu Asp Ala Ile Met Met Asn Thr Pro Val Ile Asn Ala
    370                 375                 380

Ala Val Glu Met Gly Phe Ser Arg Ser Leu Val Lys Gln Thr Val Gln
385                 390                 395                 400

Arg Lys Ile Leu Ala Thr Gly Glu Asn Tyr Arg Leu Val Asn Asp Leu
                405                 410                 415

Val Leu Asp Leu Leu Asn Ala Glu Asp Glu Ile Arg Glu Glu Glu Arg
            420                 425                 430

Glu Arg Ala Thr Glu Glu Lys Glu Ser Asn Asp Leu Leu Leu Ile Arg
        435                 440                 445

Lys Asn Arg Met Ala Leu Phe Gln His Leu Thr Cys Val Ile Pro Ile
    450                 455                 460

Leu Asp Ser Leu Leu Thr Ala Gly Ile Ile Asn Glu Gln Glu His Asp
465                 470                 475                 480
```

Val Ile Lys Gln Lys Thr Gln Thr Ser Leu Gln Ala Arg Glu Leu Ile
485 490 495

Asp Thr Ile Leu Val Lys Gly Asn Ile Ala Ala Thr Val Phe Arg Asn
500 505 510

Ser Leu Gln Glu Ala Glu Ala Val Leu Tyr Glu His Leu Phe Val Gln
515 520 525

Gln Asp Ile Lys Tyr Ile Pro Thr Glu Asp Val Ser Asp Leu Pro Val
530 535 540

Glu Glu Gln Leu Arg Arg Leu Gln Glu Glu Arg Thr Cys Lys Val Cys
545 550 555 560

Met Asp Lys Glu Val Ser Ile Val Phe Ile Pro Cys Gly His Leu Val
565 570 575

Val Cys Lys Asp Cys Ala Pro Ser Leu Arg Lys Cys Pro Ile Cys Arg
580 585 590

Ser Thr Ile Lys Gly Thr Val Arg Thr Phe Leu Ser
595 600

<210> 142
<211> 624
<212> PRT
<213> Homo sapiens

<400> 142

Met Gln Pro Asp Pro Arg Pro Ser Gly Ala Gly Ala Cys Cys Arg Phe
1 5 10 15

Leu Pro Leu Gln Ser Gln Cys Pro Glu Gly Ala Gly Asp Ala Val Met
20 25 30

Tyr Ala Ser Thr Glu Cys Lys Ala Glu Val Thr Pro Ser Gln His Gly
35 40 45

Asn Arg Thr Phe Ser Tyr Thr Leu Glu Asp His Thr Lys Gln Ala Phe
50 55 60

Gly Ile Met Asn Glu Leu Arg Leu Ser Gln Gln Leu Cys Asp Val Thr
65 70 75 80

Leu Gln Val Lys Tyr Gln Asp Ala Pro Ala Ala Gln Phe Met Ala His
85 90 95

Lys Val Val Leu Ala Ser Ser Ser Pro Val Phe Lys Ala Met Phe Thr
100 105 110

Asn Gly Leu Arg Glu Gln Gly Met Glu Val Val Ser Ile Glu Gly Ile
115 120 125

His Pro Lys Val Met Glu Arg Leu Ile Glu Phe Ala Tyr Thr Ala Ser
130 135 140

Ile Ser Met Gly Glu Lys Cys Val Leu His Val Met Asn Gly Ala Val
145 150 155 160

Met Tyr Gln Ile Asp Ser Val Val Arg Ala Cys Ser Asp Phe Leu Val
165 170 175

Gln Gln Leu Asp Pro Ser Asn Ala Ile Gly Ile Ala Asn Phe Ala Glu
180 185 190

Gln Ile Gly Cys Val Glu Leu His Gln Arg Ala Arg Glu Tyr Ile Tyr
195 200 205

Met His Phe Gly Glu Val Ala Lys Gln Glu Glu Phe Phe Asn Leu Ser
210 215 220

His Cys Gln Leu Val Thr Leu Ile Ser Arg Asp Asp Leu Asn Val Arg
225 230 235 240

Cys Glu Ser Glu Val Phe His Ala Cys Ile Asn Trp Val Lys Tyr Asp
245 250 255

Cys Glu Gln Arg Arg Phe Tyr Val Gln Ala Leu Leu Arg Ala Val Arg
260 265 270

Cys His Ser Leu Thr Pro Asn Phe Leu Gln Met Gln Leu Gln Lys Cys
275 280 285

Glu Ile Leu Gln Ser Asp Ser Arg Cys Lys Asp Tyr Leu Val Lys Ile
290 295 300

Phe Glu Glu Leu Thr Leu His Lys Pro Thr Gln Val Met Pro Cys Arg
305 310 315 320

Ala Pro Lys Val Gly Arg Leu Ile Tyr Thr Ala Gly Gly Tyr Phe Arg
325 330 335

Gln Ser Leu Ser Tyr Leu Glu Ala Tyr Asn Pro Ser Asn Gly Thr Trp
340 345 350

Leu Arg Leu Ala Asp Leu Gln Val Pro Arg Ser Gly Leu Ala Gly Cys
355 360 365

Val Val Gly Gly Leu Leu Tyr Ala Val Gly Gly Arg Asn Asn Ser Pro
370 375 380

Asp Gly Asn Thr Asp Ser Ser Ala Leu Asp Cys Tyr Asn Pro Met Thr
385 390 395 400

Asn Gln Trp Ser Pro Cys Ala Pro Met Ser Val Pro Arg Asn Arg Ile
405 410 415

Gly Val Gly Val Ile Asp Gly His Ile Tyr Ala Val Gly Gly Ser His
420 425 430

Gly Cys Ile His His Asn Ser Val Glu Arg Tyr Glu Pro Glu Arg Asp
435 440 445

Glu Trp His Leu Val Ala Pro Met Leu Thr Arg Arg Ile Gly Val Gly
450 455 460

Val Ala Val Leu Asn Arg Leu Leu Tyr Ala Val Gly Gly Phe Asp Gly
465 470 475 480

Thr Asn Arg Leu Asn Ser Ala Glu Cys Tyr Tyr Pro Glu Arg Asn Glu
485 490 495

Trp Arg Met Ile Thr Ala Met Asn Thr Ile Arg Ser Gly Ala Gly Val
500 505 510

Cys Val Leu His Asn Cys Ile Tyr Ala Ala Gly Gly Tyr Asp Gly Gln
515 520 525

Asp Gln Leu Asn Ser Val Glu Arg Tyr Asp Val Glu Thr Glu Thr Trp
530 535 540

Thr Phe Val Ala Pro Met Lys His Arg Arg Ser Ala Leu Gly Ile Thr
545 550 555 560

Val His Gln Gly Arg Ile Tyr Val Leu Gly Gly Tyr Asp Gly His Thr
565 570 575

Phe Leu Asp Ser Val Glu Cys Tyr Asp Pro Asp Thr Asp Thr Trp Ser
580 585 590

Glu Val Thr Arg Met Thr Ser Gly Arg Ser Gly Val Gly Val Ala Val
595 600 605

Thr Met Glu Pro Cys Arg Lys Gln Ile Asp Gln Gln Asn Cys Thr Cys
610 615 620

<210> 143
<211> 389
<212> PRT
<213> Homo sapiens

<400> 143

Met Leu Ser Leu Arg Val Pro Leu Ala Pro Ile Thr Asp Pro Gln Gln
1 5 10 15

Leu Gln Leu Ser Pro Leu Lys Gly Leu Ser Leu Val Asp Lys Glu Asn
20 25 30

Thr Pro Pro Ala Leu Ser Gly Thr Arg Val Leu Ala Ser Lys Thr Ala
35 40 45

Arg Arg Ile Phe Gln Glu Pro Thr Glu Pro Lys Thr Lys Ala Ala Ala
50 55 60

Pro Gly Val Glu Asp Glu Pro Leu Leu Arg Glu Asn Pro Arg Arg Phe
65 70 75 80

Val Ile Phe Pro Ile Glu Tyr His Asp Ile Trp Gln Met Tyr Lys Lys
85 90 95

Ala Glu Ala Ser Phe Trp Thr Ala Glu Glu Val Asp Leu Ser Lys Asp
100 105 110

Ile Gln His Trp Glu Ser Leu Lys Pro Glu Glu Arg Tyr Phe Ile Ser
115 120 125

His Val Leu Ala Phe Phe Ala Ala Ser Asp Gly Ile Val Asn Glu Asn
130 135 140

Leu Val Glu Arg Phe Ser Gln Glu Val Gln Ile Thr Glu Ala Arg Cys
145 150 155 160

Phe Tyr Gly Phe Gln Ile Ala Met Glu Asn Ile His Ser Glu Met Tyr
165 170 175

Ser Leu Leu Ile Asp Thr Tyr Ile Lys Asp Pro Lys Glu Arg Glu Phe
180 185 190

Leu Phe Asn Ala Ile Glu Thr Met Pro Cys Val Lys Lys Lys Ala Asp
195 200 205

Trp Ala Leu Arg Trp Ile Gly Asp Lys Glu Ala Thr Tyr Gly Glu Arg
210 215 220

Val Val Ala Phe Ala Ala Val Glu Gly Ile Phe Phe Ser Gly Ser Phe
225 230 235 240

Ala Ser Ile Phe Trp Leu Lys Lys Arg Gly Leu Met Pro Gly Leu Thr
245 250 255

Phe Ser Asn Glu Leu Ile Ser Arg Asp Glu Gly Leu His Cys Asp Phe
260 265 270

Ala Cys Leu Met Phe Lys His Leu Val His Lys Pro Ser Glu Glu Arg
275 280 285

Val Arg Glu Ile Ile Ile Asn Ala Val Arg Ile Glu Gln Glu Phe Leu
290 295 300

Thr Glu Ala Leu Pro Val Lys Leu Ile Gly Met Asn Cys Thr Leu Met
305 310 315 320

Lys Gln Tyr Ile Glu Phe Val Ala Asp Arg Leu Met Leu Glu Leu Gly
325 330 335

Phe Ser Lys Val Phe Arg Val Glu Asn Pro Phe Asp Phe Met Glu Asn
340 345 350

Ile Ser Leu Glu Gly Lys Thr Asn Phe Phe Glu Lys Arg Val Gly Glu
355 360 365

Tyr Gln Arg Met Gly Val Met Ser Ser Pro Thr Glu Asn Ser Phe Thr
370 375 380

Leu Asp Ala Asp Phe
385

<210> 144
<211> 281
<212> PRT
<213> Homo sapiens

<400> 144

Met Ala Thr Asn Phe Leu Ala His Glu Lys Ile Trp Phe Asp Lys Phe
1 5 10 15

Lys Tyr Asp Asp Ala Glu Arg Arg Phe Tyr Glu Gln Met Asn Gly Pro
20 25 30

```
Val Arg Gly Ala Ser Arg Gln Glu Asn Gly Ala Thr Val Ile Leu Arg
        35                  40                  45

Asp Ile Ala Arg Ala Arg Glu Asn Ile Gln Lys Ser Leu Ala Gly Ser
    50                  55                  60

Ser Gly Pro Gly Ala Ser Ser Gly Thr Ser Gly Asp His Gly Glu Leu
65                  70                  75                  80

Val Val Arg Ile Ala Ser Leu Glu Val Glu Asn Gln Ser Leu Arg Gly
                85                  90                  95

Val Val Gln Glu Leu Gln Gln Ala Ile Ser Lys Leu Glu Ala Arg Leu
            100                 105                 110

Asn Val Leu Glu Lys Ser Ser Pro Gly His Arg Ala Thr Ala Pro Gln
        115                 120                 125

Thr Gln His Val Ser Pro Met Arg Gln Val Glu Pro Pro Ala Lys Lys
    130                 135                 140

Pro Ala Thr Pro Ala Glu Asp Asp Glu Asp Asp Asp Ile Asp Leu Phe
145                 150                 155                 160

Gly Ser Asp Asn Glu Glu Glu Asp Lys Glu Ala Ala Gln Leu Arg Glu
                165                 170                 175

Glu Arg Leu Arg Gln Tyr Ala Glu Lys Lys Ala Lys Lys Pro Ala Leu
            180                 185                 190

Val Ala Lys Ser Ser Ile Leu Leu Asp Val Lys Pro Trp Asp Asp Glu
        195                 200                 205

Thr Asp Met Ala Gln Leu Glu Ala Cys Val Arg Ser Ile Gln Leu Asp
    210                 215                 220

Gly Leu Val Trp Gly Ala Ser Lys Leu Val Pro Val Gly Tyr Gly Ile
225                 230                 235                 240

Arg Lys Leu Gln Ile Gln Cys Val Val Glu Asp Asp Lys Val Gly Thr
                245                 250                 255

Asp Leu Leu Glu Glu Glu Ile Thr Lys Phe Glu Glu His Val Gln Ser
            260                 265                 270

Val Asp Ile Ala Ala Phe Asn Lys Ile
        275                 280
```

<210> 145
<211> 269
<212> PRT
<213> Homo sapiens

<400> 145

```
Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp
1               5                   10                  15

Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His
            20                  25                  30
```



```
Leu Val Leu Arg Leu Arg Gly Gly Met Gln Ile Phe Val Lys Thr Leu
        35                  40                  45

Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile Glu
    50                  55                  60

Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln
65                  70                  75                  80

Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu
                85                  90                  95

Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu Arg
            100                 105                 110

Leu Arg Gly Gly Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr
        115                 120                 125

Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala
    130                 135                 140

Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile
145                 150                 155                 160

Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn
                165                 170                 175

Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly
            180                 185                 190

Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu
        195                 200                 205

Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp
    210                 215                 220

Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys
225                 230                 235                 240

Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu
                245                 250                 255

Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Val
            260                 265
```

<210> 146
<211> 1231
<212> PRT
<213> Homo sapiens

<400> 146

```
Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys
1               5                   10                  15

Val Ala Glu Asp Cys Asn Glu Leu Pro Pro Arg Arg Asn Thr Glu Ile
            20                  25                  30

Leu Thr Gly Ser Trp Ser Asp Gln Thr Tyr Pro Glu Gly Thr Gln Ala
        35                  40                  45
```

```
Ile Tyr Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn Val Ile Met
    50                  55                  60

Val Cys Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu Arg Lys Cys
65                  70                  75                  80

Gln Lys Arg Pro Cys Gly His Pro Gly Asp Thr Pro Phe Gly Thr Phe
                85                  90                  95

Thr Leu Thr Gly Gly Asn Val Phe Glu Tyr Gly Val Lys Ala Val Tyr
            100                 105                 110

Thr Cys Asn Glu Gly Tyr Gln Leu Leu Gly Glu Ile Asn Tyr Arg Glu
        115                 120                 125

Cys Asp Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys Glu Val Val
    130                 135                 140

Lys Cys Leu Pro Val Thr Ala Pro Glu Asn Gly Lys Ile Val Ser Ser
145                 150                 155                 160

Ala Met Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala Val Arg Phe
                165                 170                 175

Val Cys Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu Met His Cys
            180                 185                 190

Ser Asp Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys Val Glu Ile
        195                 200                 205

Ser Cys Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile Ser Gln Lys
    210                 215                 220

Ile Ile Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys Asn Met Gly
225                 230                 235                 240

Tyr Glu Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu Ser Gly Trp
                245                 250                 255

Arg Pro Leu Pro Ser Cys Glu Glu Lys Ser Cys Asp Asn Pro Tyr Ile
            260                 265                 270

Pro Asn Gly Asp Tyr Ser Pro Leu Arg Ile Lys His Arg Thr Gly Asp
        275                 280                 285

Glu Ile Thr Tyr Gln Cys Arg Asn Gly Phe Tyr Pro Ala Thr Arg Gly
    290                 295                 300

Asn Thr Ala Lys Cys Thr Ser Thr Gly Trp Ile Pro Ala Pro Arg Cys
305                 310                 315                 320

Thr Leu Lys Pro Cys Asp Tyr Pro Asp Ile Lys His Gly Gly Leu Tyr
                325                 330                 335

His Glu Asn Met Arg Arg Pro Tyr Phe Pro Val Ala Val Gly Lys Tyr
            340                 345                 350

Tyr Ser Tyr Tyr Cys Asp Glu His Phe Glu Thr Pro Ser Gly Ser Tyr
```



```
        355                 360                 365

Trp Asp His Ile His Cys Thr Gln Asp Gly Trp Ser Pro Ala Val Pro
    370                 375                 380

Cys Leu Arg Lys Cys Tyr Phe Pro Tyr Leu Glu Asn Gly Tyr Asn Gln
385                 390                 395                 400

Asn His Gly Arg Lys Phe Val Gln Gly Lys Ser Ile Asp Val Ala Cys
                405                 410                 415

His Pro Gly Tyr Ala Leu Pro Lys Ala Gln Thr Thr Val Thr Cys Met
            420                 425                 430

Glu Asn Gly Trp Ser Pro Thr Pro Arg Cys Ile Arg Val Lys Thr Cys
        435                 440                 445

Ser Lys Ser Ser Ile Asp Ile Glu Asn Gly Phe Ile Ser Glu Ser Gln
    450                 455                 460

Tyr Thr Tyr Ala Leu Lys Glu Lys Ala Lys Tyr Gln Cys Lys Leu Gly
465                 470                 475                 480

Tyr Val Thr Ala Asp Gly Glu Thr Ser Gly Ser Ile Arg Cys Gly Lys
                485                 490                 495

Asp Gly Trp Ser Ala Gln Pro Thr Cys Ile Lys Ser Cys Asp Ile Pro
            500                 505                 510

Val Phe Met Asn Ala Arg Thr Lys Asn Asp Phe Thr Trp Phe Lys Leu
        515                 520                 525

Asn Asp Thr Leu Asp Tyr Glu Cys His Asp Gly Tyr Glu Ser Asn Thr
    530                 535                 540

Gly Ser Thr Thr Gly Ser Ile Val Cys Gly Tyr Asn Gly Trp Ser Asp
545                 550                 555                 560

Leu Pro Ile Cys Tyr Glu Arg Glu Cys Glu Leu Pro Lys Ile Asp Val
                565                 570                 575

His Leu Val Pro Asp Arg Lys Lys Asp Gln Tyr Lys Val Gly Glu Val
            580                 585                 590

Leu Lys Phe Ser Cys Lys Pro Gly Phe Thr Ile Val Gly Pro Asn Ser
        595                 600                 605

Val Gln Cys Tyr His Phe Gly Leu Ser Pro Asp Leu Pro Ile Cys Lys
    610                 615                 620

Glu Gln Val Gln Ser Cys Gly Pro Pro Pro Glu Leu Leu Asn Gly Asn
625                 630                 635                 640

Val Lys Glu Lys Thr Lys Glu Glu Tyr Gly His Ser Glu Val Val Glu
                645                 650                 655

Tyr Tyr Cys Asn Pro Arg Phe Leu Met Lys Gly Pro Asn Lys Ile Gln
            660                 665                 670
```

Cys Val Asp Gly Glu Trp Thr Thr Leu Pro Val Cys Ile Val Glu Glu
675 680 685

Ser Thr Cys Gly Asp Ile Pro Glu Leu Glu His Gly Trp Ala Gln Leu
690 695 700

Ser Ser Pro Pro Tyr Tyr Tyr Gly Asp Ser Val Glu Phe Asn Cys Ser
705 710 715 720

Glu Ser Phe Thr Met Ile Gly His Arg Ser Ile Thr Cys Ile His Gly
725 730 735

Val Trp Thr Gln Leu Pro Gln Cys Val Ala Ile Asp Lys Leu Lys Lys
740 745 750

Cys Lys Ser Ser Asn Leu Ile Ile Leu Glu Glu His Leu Lys Asn Lys
755 760 765

Lys Glu Phe Asp His Asn Ser Asn Ile Arg Tyr Arg Cys Arg Gly Lys
770 775 780

Glu Gly Trp Ile His Thr Val Cys Ile Asn Gly Arg Trp Asp Pro Glu
785 790 795 800

Val Asn Cys Ser Met Ala Gln Ile Gln Leu Cys Pro Pro Pro Pro Gln
805 810 815

Ile Pro Asn Ser His Asn Met Thr Thr Thr Leu Asn Tyr Arg Asp Gly
820 825 830

Glu Lys Val Ser Val Leu Cys Gln Glu Asn Tyr Leu Ile Gln Glu Gly
835 840 845

Glu Glu Ile Thr Cys Lys Asp Gly Arg Trp Gln Ser Ile Pro Leu Cys
850 855 860

Val Glu Lys Ile Pro Cys Ser Gln Pro Pro Gln Ile Glu His Gly Thr
865 870 875 880

Ile Asn Ser Ser Arg Ser Ser Gln Glu Ser Tyr Ala His Gly Thr Lys
885 890 895

Leu Ser Tyr Thr Cys Glu Gly Gly Phe Arg Ile Ser Glu Glu Asn Glu
900 905 910

Thr Thr Cys Tyr Met Gly Lys Trp Ser Ser Pro Pro Gln Cys Glu Gly
915 920 925

Leu Pro Cys Lys Ser Pro Pro Glu Ile Ser His Gly Val Val Ala His
930 935 940

Met Ser Asp Ser Tyr Gln Tyr Gly Glu Glu Val Thr Tyr Lys Cys Phe
945 950 955 960

Glu Gly Phe Gly Ile Asp Gly Pro Ala Ile Ala Lys Cys Leu Gly Glu
965 970 975

Lys Trp Ser His Pro Pro Ser Cys Ile Lys Thr Asp Cys Leu Ser Leu
980 985 990

Pro Ser Phe Glu Asn Ala Ile Pro Met Gly Glu Lys Lys Asp Val Tyr
995 1000 1005

Lys Ala Gly Glu Gln Val Thr Tyr Thr Cys Ala Thr Tyr Tyr Lys
1010 1015 1020

Met Asp Gly Ala Ser Asn Val Thr Cys Ile Asn Ser Arg Trp Thr
1025 1030 1035

Gly Arg Pro Thr Cys Arg Asp Thr Ser Cys Val Asn Pro Pro Thr
1040 1045 1050

Val Gln Asn Ala Tyr Ile Val Ser Arg Gln Met Ser Lys Tyr Pro
1055 1060 1065

Ser Gly Glu Arg Val Arg Tyr Gln Cys Arg Ser Pro Tyr Glu Met
1070 1075 1080

Phe Gly Asp Glu Glu Val Met Cys Leu Asn Gly Asn Trp Thr Glu
1085 1090 1095

Pro Pro Gln Cys Lys Asp Ser Thr Gly Lys Cys Gly Pro Pro Pro
1100 1105 1110

Pro Ile Asp Asn Gly Asp Ile Thr Ser Phe Pro Leu Ser Val Tyr
1115 1120 1125

Ala Pro Ala Ser Ser Val Glu Tyr Gln Cys Gln Asn Leu Tyr Gln
1130 1135 1140

Leu Glu Gly Asn Lys Arg Ile Thr Cys Arg Asn Gly Gln Trp Ser
1145 1150 1155

Glu Pro Pro Lys Cys Leu His Pro Cys Val Ile Ser Arg Glu Ile
1160 1165 1170

Met Glu Asn Tyr Asn Ile Ala Leu Arg Trp Thr Ala Lys Gln Lys
1175 1180 1185

Leu Tyr Ser Arg Thr Gly Glu Ser Val Glu Phe Val Cys Lys Arg
1190 1195 1200

Gly Tyr Arg Leu Ser Ser Arg Ser His Thr Leu Arg Thr Thr Cys
1205 1210 1215

Trp Asp Gly Lys Leu Glu Tyr Pro Thr Cys Ala Lys Arg
1220 1225 1230

<210> 147
<211> 364
<212> PRT
<213> Homo sapiens

<400> 147

Met Tyr Leu Ser Arg Phe Leu Ser Ile His Ala Leu Trp Val Thr Val
1 5 10 15

Ser Ser Val Met Gln Pro Tyr Pro Leu Val Trp Gly His Tyr Asp Leu
20 25 30

```
Cys Lys Thr Gln Ile Tyr Thr Glu Glu Gly Lys Val Trp Asp Tyr Met
        35                  40                  45

Ala Cys Gln Pro Glu Ser Thr Asp Met Thr Lys Tyr Leu Lys Val Lys
    50                  55                  60

Leu Asp Pro Pro Asp Ile Thr Cys Gly Asp Pro Pro Glu Thr Phe Cys
65                  70                  75                  80

Ala Met Gly Asn Pro Tyr Met Cys Asn Asn Glu Cys Asp Ala Ser Thr
                85                  90                  95

Pro Glu Leu Ala His Pro Pro Glu Leu Met Phe Asp Phe Glu Gly Arg
            100                 105                 110

His Pro Ser Thr Phe Trp Gln Ser Ala Thr Trp Lys Glu Tyr Pro Lys
        115                 120                 125

Pro Leu Gln Val Asn Ile Thr Leu Ser Trp Ser Lys Thr Ile Glu Leu
    130                 135                 140

Thr Asp Asn Ile Val Ile Thr Phe Glu Ser Gly Arg Pro Asp Gln Met
145                 150                 155                 160

Ile Leu Glu Lys Ser Leu Asp Tyr Gly Arg Thr Trp Gln Pro Tyr Gln
                165                 170                 175

Tyr Tyr Ala Thr Asp Cys Leu Asp Ala Phe His Met Asp Pro Lys Ser
            180                 185                 190

Val Lys Asp Leu Ser Gln His Thr Val Leu Glu Ile Ile Cys Thr Glu
        195                 200                 205

Glu Tyr Ser Thr Gly Tyr Thr Thr Asn Ser Lys Ile Ile His Phe Glu
    210                 215                 220

Ile Lys Asp Arg Phe Ala Phe Phe Ala Gly Pro Arg Leu Arg Asn Met
225                 230                 235                 240

Ala Ser Leu Tyr Gly Gln Leu Asp Thr Thr Lys Lys Leu Arg Asp Phe
                245                 250                 255

Phe Thr Val Thr Asp Leu Arg Ile Arg Leu Leu Arg Pro Ala Val Gly
            260                 265                 270

Glu Ile Phe Val Asp Glu Leu His Leu Ala Arg Tyr Phe Tyr Ala Ile
        275                 280                 285

Ser Asp Ile Lys Val Arg Gly Arg Cys Lys Cys Asn Leu His Ala Thr
    290                 295                 300

Val Cys Val Tyr Asp Asn Ser Lys Leu Thr Cys Glu Cys Glu His Asn
305                 310                 315                 320

Thr Thr Gly Pro Asp Cys Gly Lys Cys Lys Lys Asn Tyr Gln Gly Arg
                325                 330                 335

Pro Trp Ser Pro Gly Ser Tyr Leu Pro Ile Pro Lys Gly Thr Ala Asn
            340                 345                 350
```



```
Thr Cys Ile Pro Ser Ile Ser Ser Ile Gly Ser Lys
        355                 360
```

<210> 148
<211> 3210
<212> PRT
<213> Homo sapiens

<400> 148

```
Met Ser Trp Ala Leu Glu Glu Trp Lys Glu Gly Leu Pro Thr Arg Thr
1               5                   10                  15

Leu Gln Lys Ile Gln Glu Leu Glu Gly Gln Leu Asp Lys Leu Lys Lys
            20                  25                  30

Glu Lys Gln Gln Arg Gln Phe Gln Leu Asp Ser Leu Glu Ala Ala Pro
        35                  40                  45

Gln Lys Gln Thr Gln Lys Val Glu Asn Glu Lys Thr Glu Gly Thr Asn
    50                  55                  60

Leu Lys Arg Glu Asn Gln Arg Leu Met Glu Ile Cys Glu Ser Leu Glu
65                  70                  75                  80

Lys Thr Lys Gln Lys Ile Ser His Glu Leu Gln Val Lys Glu Ser Gln
                85                  90                  95

Val Asn Phe Gln Glu Gly Gln Leu Asn Ser Gly Lys Lys Gln Ile Glu
            100                 105                 110

Lys Leu Glu Gln Glu Leu Lys Arg Cys Lys Ser Glu Leu Glu Arg Ser
        115                 120                 125

Gln Gln Ala Ala Gln Ser Ala Asp Val Ser Leu Asn Pro Cys Asn Thr
    130                 135                 140

Pro Gln Lys Ile Phe Thr Thr Pro Leu Thr Pro Ser Gln Tyr Tyr Ser
145                 150                 155                 160

Gly Ser Lys Tyr Glu Asp Leu Lys Glu Lys Tyr Asn Lys Glu Val Glu
                165                 170                 175

Glu Arg Lys Arg Leu Glu Ala Glu Val Lys Ala Leu Gln Ala Lys Lys
            180                 185                 190

Ala Ser Gln Thr Leu Pro Gln Ala Thr Met Asn His Arg Asp Ile Ala
        195                 200                 205

Arg His Gln Ala Ser Ser Ser Val Phe Ser Trp Gln Gln Glu Lys Thr
    210                 215                 220

Pro Ser His Leu Ser Ser Asn Ser Gln Arg Thr Pro Ile Arg Arg Asp
225                 230                 235                 240

Phe Ser Ala Ser Tyr Phe Ser Gly Glu Leu Glu Val Thr Pro Ser Arg
                245                 250                 255

Ser Thr Leu Gln Ile Gly Lys Arg Asp Ala Asn Ser Ser Phe Phe Gly
            260                 265                 270
```

```
Asn Ser Ser Ser Pro His Leu Leu Asp Gln Leu Lys Ala Gln Asn Gln
        275                 280                 285

Glu Leu Arg Asn Lys Ile Asn Glu Leu Glu Leu Arg Leu Gln Gly His
    290                 295                 300

Glu Lys Glu Met Lys Gly Gln Val Asn Lys Phe Gln Glu Leu Gln Leu
305                 310                 315                 320

Gln Leu Glu Lys Ala Lys Val Glu Leu Ile Glu Lys Glu Lys Val Leu
                325                 330                 335

Asn Lys Cys Arg Asp Glu Leu Val Arg Thr Thr Ala Gln Tyr Asp Gln
            340                 345                 350

Ala Ser Thr Lys Tyr Thr Ala Leu Glu Gln Lys Leu Lys Lys Leu Thr
        355                 360                 365

Glu Asp Leu Ser Cys Gln Arg Gln Asn Ala Glu Ser Ala Arg Cys Ser
    370                 375                 380

Leu Glu Gln Lys Ile Lys Glu Lys Glu Lys Glu Phe Gln Glu Glu Leu
385                 390                 395                 400

Ser Arg Gln Gln Arg Ser Phe Gln Thr Leu Asp Gln Glu Cys Ile Gln
                405                 410                 415

Met Lys Ala Arg Leu Thr Gln Glu Leu Gln Gln Ala Lys Asn Met His
            420                 425                 430

Asn Val Leu Gln Ala Glu Leu Asp Lys Leu Thr Ser Val Lys Gln Gln
        435                 440                 445

Leu Glu Asn Asn Leu Glu Glu Phe Lys Gln Lys Leu Cys Arg Ala Glu
    450                 455                 460

Gln Ala Phe Gln Ala Ser Gln Ile Lys Glu Asn Glu Leu Arg Arg Ser
465                 470                 475                 480

Met Glu Glu Met Lys Lys Glu Asn Asn Leu Leu Lys Ser His Ser Glu
                485                 490                 495

Gln Lys Ala Arg Glu Val Cys His Leu Glu Ala Glu Leu Lys Asn Ile
            500                 505                 510

Lys Gln Cys Leu Asn Gln Ser Gln Asn Phe Ala Glu Glu Met Lys Ala
        515                 520                 525

Lys Asn Thr Ser Gln Glu Thr Met Leu Arg Asp Leu Gln Glu Lys Ile
    530                 535                 540

Asn Gln Gln Glu Asn Ser Leu Thr Leu Glu Lys Leu Lys Leu Ala Val
545                 550                 555                 560

Ala Asp Leu Glu Lys Gln Arg Asp Cys Ser Gln Asp Leu Leu Lys Lys
                565                 570                 575

Arg Glu His His Ile Glu Gln Leu Asn Asp Lys Leu Ser Lys Thr Glu
```



```
            580                 585                 590

Lys Glu Ser Lys Ala Leu Leu Ser Ala Leu Glu Leu Lys Lys Lys Glu
        595                 600                 605

Tyr Glu Glu Leu Lys Glu Glu Lys Thr Leu Phe Ser Cys Trp Lys Ser
    610                 615                 620

Glu Asn Glu Lys Leu Leu Thr Gln Met Glu Ser Glu Lys Glu Asn Leu
625                 630                 635                 640

Gln Ser Lys Ile Asn His Leu Glu Thr Cys Leu Lys Thr Gln Gln Ile
                645                 650                 655

Lys Ser His Glu Tyr Asn Glu Arg Val Arg Thr Leu Glu Met Asp Arg
            660                 665                 670

Glu Asn Leu Ser Val Glu Ile Arg Asn Leu His Asn Val Leu Asp Ser
        675                 680                 685

Lys Ser Val Glu Val Glu Thr Gln Lys Leu Ala Tyr Met Glu Leu Gln
    690                 695                 700

Gln Lys Ala Glu Phe Ser Asp Gln Lys His Gln Lys Glu Ile Glu Asn
705                 710                 715                 720

Met Cys Leu Lys Thr Ser Gln Leu Thr Gly Gln Val Glu Asp Leu Glu
                725                 730                 735

His Lys Leu Gln Leu Leu Ser Asn Glu Ile Met Asp Lys Asp Arg Cys
            740                 745                 750

Tyr Gln Asp Leu His Ala Glu Tyr Glu Ser Leu Arg Asp Leu Leu Lys
        755                 760                 765

Ser Lys Asp Ala Ser Leu Val Thr Asn Glu Asp His Gln Arg Ser Leu
    770                 775                 780

Leu Ala Phe Asp Gln Gln Pro Ala Met His His Ser Phe Ala Asn Ile
785                 790                 795                 800

Ile Gly Glu Gln Gly Ser Met Pro Ser Glu Arg Ser Glu Cys Arg Leu
                805                 810                 815

Glu Ala Asp Gln Ser Pro Lys Asn Ser Ala Ile Leu Gln Asn Arg Val
            820                 825                 830

Asp Ser Leu Glu Phe Ser Leu Glu Ser Gln Lys Gln Met Asn Ser Asp
        835                 840                 845

Leu Gln Lys Gln Cys Glu Glu Leu Val Gln Ile Lys Gly Glu Ile Glu
    850                 855                 860

Glu Asn Leu Met Lys Ala Glu Gln Met His Gln Ser Phe Val Ala Glu
865                 870                 875                 880

Thr Ser Gln Arg Ile Ser Lys Leu Gln Glu Asp Thr Ser Ala His Gln
                885                 890                 895
```

Asn Val Val Ala Glu Thr Leu Ser Ala Leu Glu Asn Lys Glu Lys Glu
900 905 910

Leu Gln Leu Leu Asn Asp Lys Val Glu Thr Glu Gln Ala Glu Ile Gln
915 920 925

Glu Leu Lys Lys Ser Asn His Leu Leu Glu Asp Ser Leu Lys Glu Leu
930 935 940

Gln Leu Leu Ser Glu Thr Leu Ser Leu Glu Lys Lys Glu Met Ser Ser
945 950 955 960

Ile Ile Ser Leu Asn Lys Arg Glu Ile Glu Glu Leu Thr Gln Glu Asn
965 970 975

Gly Thr Leu Lys Glu Ile Asn Ala Ser Leu Asn Gln Glu Lys Met Asn
980 985 990

Leu Ile Gln Lys Ser Glu Ser Phe Ala Asn Tyr Ile Asp Glu Arg Glu
995 1000 1005

Lys Ser Ile Ser Glu Leu Ser Asp Gln Tyr Lys Gln Glu Lys Leu
1010 1015 1020

Ile Leu Leu Gln Arg Cys Glu Glu Thr Gly Asn Ala Tyr Glu Asp
1025 1030 1035

Leu Ser Gln Lys Tyr Lys Ala Ala Gln Glu Lys Asn Ser Lys Leu
1040 1045 1050

Glu Cys Leu Leu Asn Glu Cys Thr Ser Leu Cys Glu Asn Arg Lys
1055 1060 1065

Asn Glu Leu Glu Gln Leu Lys Glu Ala Phe Ala Lys Glu His Gln
1070 1075 1080

Glu Phe Leu Thr Lys Leu Ala Phe Ala Glu Glu Arg Asn Gln Asn
1085 1090 1095

Leu Met Leu Glu Leu Glu Thr Val Gln Gln Ala Leu Arg Ser Glu
1100 1105 1110

Met Thr Asp Asn Gln Asn Asn Ser Lys Ser Glu Ala Gly Gly Leu
1115 1120 1125

Lys Gln Glu Ile Met Thr Leu Lys Glu Glu Gln Asn Lys Met Gln
1130 1135 1140

Lys Glu Val Asn Asp Leu Leu Gln Glu Asn Glu Gln Leu Met Lys
1145 1150 1155

Val Met Lys Thr Lys His Glu Cys Gln Asn Leu Glu Ser Glu Pro
1160 1165 1170

Ile Arg Asn Ser Val Lys Glu Arg Glu Ser Glu Arg Asn Gln Cys
1175 1180 1185

Asn Phe Lys Pro Gln Met Asp Leu Glu Val Lys Glu Ile Ser Leu
1190 1195 1200

Asp Ser Tyr Asn Ala Gln Leu Val Gln Leu Glu Ala Met Leu Arg
1205 1210 1215

Asn Lys Glu Leu Lys Leu Gln Glu Ser Glu Lys Glu Lys Glu Cys
1220 1225 1230

Leu Gln His Glu Leu Gln Thr Ile Arg Gly Asp Leu Glu Thr Ser
1235 1240 1245

Asn Leu Gln Asp Met Gln Ser Gln Glu Ile Ser Gly Leu Lys Asp
1250 1255 1260

Cys Glu Ile Asp Ala Glu Glu Lys Tyr Ile Ser Gly Pro His Glu
1265 1270 1275

Leu Ser Thr Ser Gln Asn Asp Asn Ala His Leu Gln Cys Ser Leu
1280 1285 1290

Gln Thr Thr Met Asn Lys Leu Asn Glu Leu Glu Lys Ile Cys Glu
1295 1300 1305

Ile Leu Gln Ala Glu Lys Tyr Glu Leu Val Thr Glu Leu Asn Asp
1310 1315 1320

Ser Arg Ser Glu Cys Ile Thr Ala Thr Arg Lys Met Ala Glu Glu
1325 1330 1335

Val Gly Lys Leu Leu Asn Glu Val Lys Ile Leu Asn Asp Asp Ser
1340 1345 1350

Gly Leu Leu His Gly Glu Leu Val Glu Asp Ile Pro Gly Gly Glu
1355 1360 1365

Phe Gly Glu Gln Pro Asn Glu Gln His Pro Val Ser Leu Ala Pro
1370 1375 1380

Leu Asp Glu Ser Asn Ser Tyr Glu His Leu Thr Leu Ser Asp Lys
1385 1390 1395

Glu Val Gln Met His Phe Ala Glu Leu Gln Glu Lys Phe Leu Ser
1400 1405 1410

Leu Gln Ser Glu His Lys Ile Leu His Asp Gln His Cys Gln Met
1415 1420 1425

Ser Ser Lys Met Ser Glu Leu Gln Thr Tyr Val Asp Ser Leu Lys
1430 1435 1440

Ala Glu Asn Leu Val Leu Ser Thr Asn Leu Arg Asn Phe Gln Gly
1445 1450 1455

Asp Leu Val Lys Glu Met Gln Leu Gly Leu Glu Glu Gly Leu Val
1460 1465 1470

Pro Ser Leu Ser Ser Ser Cys Val Pro Asp Ser Ser Ser Leu Ser
1475 1480 1485

Ser Leu Gly Asp Ser Ser Phe Tyr Arg Ala Leu Leu Glu Gln Thr
1490 1495 1500

```
Gly Asp Met Ser Leu Leu Ser Asn Leu Glu Gly Ala Val Ser Ala
1505                1510                1515

Asn Glu Cys Ser Val Asp Glu Val Phe Cys Ser Ser Leu Gln Thr
1520                1525                1530

Tyr Val Asp Ser Leu Lys Ala Glu Asn Leu Val Leu Ser Thr Asn
1535                1540                1545

Leu Arg Asn Phe Gln Gly Asp Leu Val Lys Glu Met Gln Leu Gly
1550                1555                1560

Leu Glu Glu Gly Leu Val Pro Ser Leu Ser Ser Ser Cys Val Pro
1565                1570                1575

Asp Ser Ser Ser Leu Ser Ser Leu Gly Asp Ser Ser Phe Tyr Arg
1580                1585                1590

Ala Leu Leu Glu Gln Thr Gly Asp Met Ser Leu Leu Ser Asn Leu
1595                1600                1605

Glu Gly Val Val Ser Ala Asn Gln Cys Ser Val Asp Glu Val Phe
1610                1615                1620

Cys Ser Ser Leu Gln Glu Glu Asn Leu Thr Arg Lys Glu Thr Pro
1625                1630                1635

Ser Ala Pro Ala Lys Gly Val Glu Glu Leu Glu Ser Leu Cys Glu
1640                1645                1650

Val Tyr Arg Gln Ser Leu Glu Lys Leu Glu Glu Lys Met Glu Ser
1655                1660                1665

Gln Gly Ile Met Lys Asn Lys Glu Ile Gln Glu Leu Glu Gln Leu
1670                1675                1680

Leu Ser Ser Glu Arg Gln Glu Leu Asp Cys Leu Arg Lys Gln Tyr
1685                1690                1695

Leu Ser Glu Asn Glu Gln Trp Gln Gln Lys Leu Thr Ser Val Thr
1700                1705                1710

Leu Glu Met Glu Ser Lys Leu Ala Ala Glu Lys Lys Gln Thr Glu
1715                1720                1725

Gln Leu Ser Leu Glu Leu Glu Val Ala Arg Leu Gln Leu Gln Gly
1730                1735                1740

Leu Asp Leu Ser Ser Arg Ser Leu Leu Gly Ile Asp Thr Glu Asp
1745                1750                1755

Ala Ile Gln Gly Arg Asn Glu Ser Cys Asp Ile Ser Lys Glu His
1760                1765                1770

Thr Ser Glu Thr Thr Glu Arg Thr Pro Lys His Asp Val His Gln
1775                1780                1785

Ile Cys Asp Lys Asp Ala Gln Gln Asp Leu Asn Leu Asp Ile Glu
```



```
1790                1795                1800

Lys Ile Thr Glu Thr Gly Ala Val Lys Pro Thr Gly Glu Cys Ser
1805                1810                1815

Gly Glu Gln Ser Pro Asp Thr Asn Tyr Glu Pro Pro Gly Glu Asp
1820                1825                1830

Lys Thr Gln Gly Ser Ser Glu Cys Ile Ser Glu Leu Ser Phe Ser
1835                1840                1845

Gly Pro Asn Ala Leu Val Pro Met Asp Phe Leu Gly Asn Gln Glu
1850                1855                1860

Asp Ile His Asn Leu Gln Leu Arg Val Lys Glu Thr Ser Asn Glu
1865                1870                1875

Asn Leu Arg Leu Leu His Val Ile Glu Asp Arg Asp Arg Lys Val
1880                1885                1890

Glu Ser Leu Leu Asn Glu Met Lys Glu Leu Asp Ser Lys Leu His
1895                1900                1905

Leu Gln Glu Val Gln Leu Met Thr Lys Ile Glu Ala Cys Ile Glu
1910                1915                1920

Leu Glu Lys Ile Val Gly Glu Leu Lys Lys Glu Asn Ser Asp Leu
1925                1930                1935

Ser Glu Lys Leu Glu Tyr Phe Ser Cys Asp His Gln Glu Leu Leu
1940                1945                1950

Gln Arg Val Glu Thr Ser Glu Gly Leu Asn Ser Asp Leu Glu Met
1955                1960                1965

His Ala Asp Lys Ser Ser Arg Glu Asp Ile Gly Asp Asn Val Ala
1970                1975                1980

Lys Val Asn Asp Ser Trp Lys Glu Arg Phe Leu Asp Val Glu Asn
1985                1990                1995

Glu Leu Ser Arg Ile Arg Ser Glu Lys Ala Ser Ile Glu His Glu
2000                2005                2010

Ala Leu Tyr Leu Glu Ala Asp Leu Glu Val Val Gln Thr Glu Lys
2015                2020                2025

Leu Cys Leu Glu Lys Asp Asn Glu Asn Lys Gln Lys Val Ile Val
2030                2035                2040

Cys Leu Glu Glu Glu Leu Ser Val Val Thr Ser Glu Arg Asn Gln
2045                2050                2055

Leu Arg Gly Glu Leu Asp Thr Met Ser Lys Lys Thr Thr Ala Leu
2060                2065                2070

Asp Gln Leu Ser Glu Lys Met Lys Glu Lys Thr Gln Glu Leu Glu
2075                2080                2085
```

Ser His Gln Ser Glu Cys Leu His Cys Ile Gln Val Ala Glu Ala
2090 2095 2100

Glu Val Lys Glu Lys Thr Glu Leu Leu Gln Thr Leu Ser Ser Asp
2105 2110 2115

Val Ser Glu Leu Leu Lys Asp Lys Thr His Leu Gln Glu Lys Leu
2120 2125 2130

Gln Ser Leu Glu Lys Asp Ser Gln Ala Leu Ser Leu Thr Lys Cys
2135 2140 2145

Glu Leu Glu Asn Gln Ile Ala Gln Leu Asn Lys Glu Lys Glu Leu
2150 2155 2160

Leu Val Lys Glu Ser Glu Ser Leu Gln Ala Arg Leu Ser Glu Ser
2165 2170 2175

Asp Tyr Glu Lys Leu Asn Val Ser Lys Ala Leu Glu Ala Ala Leu
2180 2185 2190

Val Glu Lys Gly Glu Phe Ala Leu Arg Leu Ser Ser Thr Gln Glu
2195 2200 2205

Glu Val His Gln Leu Arg Arg Gly Ile Glu Lys Leu Arg Val Arg
2210 2215 2220

Ile Glu Ala Asp Glu Lys Lys Gln Leu His Ile Ala Glu Lys Leu
2225 2230 2235

Lys Glu Arg Glu Arg Glu Asn Asp Ser Leu Lys Asp Lys Val Glu
2240 2245 2250

Asn Leu Glu Arg Glu Leu Gln Met Ser Glu Glu Asn Gln Glu Leu
2255 2260 2265

Val Ile Leu Asp Ala Glu Asn Ser Lys Ala Glu Val Glu Thr Leu
2270 2275 2280

Lys Thr Gln Ile Glu Glu Met Ala Arg Ser Leu Lys Val Phe Glu
2285 2290 2295

Leu Asp Leu Val Thr Leu Arg Ser Glu Lys Glu Asn Leu Thr Lys
2300 2305 2310

Gln Ile Gln Glu Lys Gln Gly Gln Leu Ser Glu Leu Asp Lys Leu
2315 2320 2325

Leu Ser Ser Phe Lys Ser Leu Leu Glu Glu Lys Glu Gln Ala Glu
2330 2335 2340

Ile Gln Ile Lys Glu Glu Ser Lys Thr Ala Val Glu Met Leu Gln
2345 2350 2355

Asn Gln Leu Lys Glu Leu Asn Glu Ala Val Ala Ala Leu Cys Gly
2360 2365 2370

Asp Gln Glu Ile Met Lys Ala Thr Glu Gln Ser Leu Asp Pro Pro
2375 2380 2385

Ile Glu Glu Glu His Gln Leu Arg Asn Ser Ile Glu Lys Leu Arg
2390 2395 2400

Ala Arg Leu Glu Ala Asp Glu Lys Lys Gln Leu Cys Val Leu Gln
2405 2410 2415

Gln Leu Lys Glu Ser Glu His His Ala Asp Leu Leu Lys Gly Arg
2420 2425 2430

Val Glu Asn Leu Glu Arg Glu Leu Glu Ile Ala Arg Thr Asn Gln
2435 2440 2445

Glu His Ala Ala Leu Glu Ala Glu Asn Ser Lys Gly Glu Val Glu
2450 2455 2460

Thr Leu Lys Ala Lys Ile Glu Gly Met Thr Gln Ser Leu Arg Gly
2465 2470 2475

Leu Glu Leu Asp Val Val Thr Ile Arg Ser Glu Lys Glu Asp Leu
2480 2485 2490

Thr Asn Glu Leu Gln Lys Glu Gln Glu Arg Ile Ser Glu Leu Glu
2495 2500 2505

Ile Ile Asn Ser Ser Phe Glu Asn Ile Leu Gln Glu Lys Glu Gln
2510 2515 2520

Glu Lys Val Gln Met Lys Glu Lys Ser Ser Thr Ala Met Glu Met
2525 2530 2535

Leu Gln Thr Gln Leu Lys Glu Leu Asn Glu Arg Val Ala Ala Leu
2540 2545 2550

His Asn Asp Gln Glu Ala Cys Lys Ala Lys Glu Gln Asn Leu Ser
2555 2560 2565

Ser Gln Val Glu Cys Leu Glu Leu Glu Lys Ala Gln Leu Leu Gln
2570 2575 2580

Gly Leu Asp Glu Ala Lys Asn Asn Tyr Ile Val Leu Gln Ser Ser
2585 2590 2595

Val Asn Gly Leu Ile Gln Glu Val Glu Asp Gly Lys Gln Lys Leu
2600 2605 2610

Glu Lys Lys Asp Glu Glu Ile Ser Arg Leu Lys Asn Gln Ile Gln
2615 2620 2625

Asp Gln Glu Gln Leu Val Ser Lys Leu Ser Gln Val Glu Gly Glu
2630 2635 2640

His Gln Leu Trp Lys Glu Gln Asn Leu Glu Leu Arg Asn Leu Thr
2645 2650 2655

Val Glu Leu Glu Gln Lys Ile Gln Val Leu Gln Ser Lys Asn Ala
2660 2665 2670

Ser Leu Gln Asp Thr Leu Glu Val Leu Gln Ser Ser Tyr Lys Asn
2675 2680 2685

```
Leu Glu  Asn Glu Leu Glu Leu  Thr Lys Met Asp Lys  Met Ser Phe
    2690                 2695                 2700

Val Glu  Lys Val Asn Lys Met  Thr Ala Lys Glu Thr  Glu Leu Gln
    2705                 2710                 2715

Arg Glu  Met His Glu Met Ala  Gln Lys Thr Ala Glu  Leu Gln Glu
    2720                 2725                 2730

Glu Leu  Ser Gly Glu Lys Asn  Arg Leu Ala Gly Glu  Leu Gln Leu
    2735                 2740                 2745

Leu Leu  Glu Glu Ile Lys Ser  Ser Lys Asp Gln Leu  Lys Glu Leu
    2750                 2755                 2760

Thr Leu  Glu Asn Ser Glu Leu  Lys Lys Ser Leu Asp  Cys Met His
    2765                 2770                 2775

Lys Asp  Gln Val Glu Lys Glu  Gly Lys Val Arg Glu  Glu Ile Ala
    2780                 2785                 2790

Glu Tyr  Gln Leu Arg Leu His  Glu Ala Glu Lys Lys  His Gln Ala
    2795                 2800                 2805

Leu Leu  Leu Asp Thr Asn Lys  Gln Tyr Glu Val Glu  Ile Gln Thr
    2810                 2815                 2820

Tyr Arg  Glu Lys Leu Thr Ser  Lys Glu Glu Cys Leu  Ser Ser Gln
    2825                 2830                 2835

Lys Leu  Glu Ile Asp Leu Leu  Lys Ser Ser Lys Glu  Glu Leu Asn
    2840                 2845                 2850

Asn Ser  Leu Lys Ala Thr Thr  Gln Ile Leu Glu Glu  Leu Lys Lys
    2855                 2860                 2865

Thr Lys  Met Asp Asn Leu Lys  Tyr Val Asn Gln Leu  Lys Lys Glu
    2870                 2875                 2880

Asn Glu  Arg Ala Gln Gly Lys  Met Lys Leu Leu Ile  Lys Ser Cys
    2885                 2890                 2895

Lys Gln  Leu Glu Glu Glu Lys  Glu Ile Leu Gln Lys  Glu Leu Ser
    2900                 2905                 2910

Gln Leu  Gln Ala Ala Gln Glu  Lys Gln Lys Thr Gly  Thr Val Met
    2915                 2920                 2925

Asp Thr  Lys Val Asp Glu Leu  Thr Thr Glu Ile Lys  Glu Leu Lys
    2930                 2935                 2940

Glu Thr  Leu Glu Glu Lys Thr  Lys Glu Ala Asp Glu  Tyr Leu Asp
    2945                 2950                 2955

Lys Tyr  Cys Ser Leu Leu Ile  Ser His Glu Lys Leu  Glu Lys Ala
    2960                 2965                 2970

Lys Glu  Met Leu Glu Thr Gln  Val Ala His Leu Cys  Ser Gln Gln
```



```
    2975                 2980                 2985

Ser Lys  Gln Asp Ser Arg Gly  Ser Pro Leu Leu Gly  Pro Val Val
    2990                 2995                 3000

Pro Gly  Pro Ser Pro Ile Pro  Ser Val Thr Glu Lys  Arg Leu Ser
    3005                 3010                 3015

Ser Gly  Gln Asn Lys Ala Ser  Gly Lys Arg Gln Arg  Ser Ser Gly
    3020                 3025                 3030

Ile Trp  Glu Asn Gly Gly Gly  Pro Thr Pro Ala Thr  Pro Glu Ser
    3035                 3040                 3045

Phe Ser  Lys Lys Ser Lys Lys  Ala Val Met Ser Gly  Ile His Pro
    3050                 3055                 3060

Ala Glu  Asp Thr Glu Gly Thr  Glu Phe Glu Pro Glu  Gly Leu Pro
    3065                 3070                 3075

Glu Val  Val Lys Lys Gly Phe  Ala Asp Ile Pro Thr  Gly Lys Thr
    3080                 3085                 3090

Ser Pro  Tyr Ile Leu Arg Arg  Thr Thr Met Ala Thr  Arg Thr Ser
    3095                 3100                 3105

Pro Arg  Leu Ala Ala Gln Lys  Leu Ala Leu Ser Pro  Leu Ser Leu
    3110                 3115                 3120

Gly Lys  Glu Asn Leu Ala Glu  Ser Ser Lys Pro Thr  Ala Gly Gly
    3125                 3130                 3135

Ser Arg  Ser Gln Lys Val Lys  Val Ala Gln Arg Ser  Pro Val Asp
    3140                 3145                 3150

Ser Gly  Thr Ile Leu Arg Glu  Pro Thr Thr Lys Ser  Val Pro Val
    3155                 3160                 3165

Asn Asn  Leu Pro Glu Arg Ser  Pro Thr Asp Ser Pro  Arg Glu Gly
    3170                 3175                 3180

Leu Arg  Val Lys Arg Gly Arg  Leu Val Pro Ser Pro  Lys Ala Gly
    3185                 3190                 3195

Leu Glu  Ser Lys Gly Ser Glu  Asn Cys Lys Val Gln
    3200                 3205                 3210
```

<210> 149
<211> 108
<212> PRT
<213> Homo sapiens

<400> 149

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Phe Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
```

```
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu
            100                 105
```

<210> 150
<211> 253
<212> PRT
<213> Homo sapiens

<400> 150

```
Met Ala Arg Ser Leu Leu Leu Pro Leu Gln Ile Leu Leu Leu Ser Leu
1               5                   10                  15

Ala Leu Glu Thr Ala Gly Glu Glu Ala Gln Gly Asp Lys Ile Ile Asp
            20                  25                  30

Gly Ala Pro Cys Ala Arg Gly Ser His Pro Trp Gln Val Ala Leu Leu
        35                  40                  45

Ser Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn Glu Arg Trp
    50                  55                  60

Val Leu Thr Ala Ala His Cys Lys Met Asn Glu Tyr Thr Val His Leu
65                  70                  75                  80

Gly Ser Asp Thr Leu Gly Asp Arg Arg Ala Gln Arg Ile Lys Ala Ser
                85                  90                  95

Lys Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His Val Asn Asp
            100                 105                 110

Leu Met Leu Val Lys Leu Asn Ser Gln Ala Arg Leu Ser Ser Met Val
        115                 120                 125

Lys Lys Val Arg Leu Pro Ser Arg Cys Glu Pro Pro Gly Thr Thr Cys
    130                 135                 140

Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro
145                 150                 155                 160

Ser Asp Leu Met Cys Val Asp Val Lys Leu Ile Ser Pro Gln Asp Cys
                165                 170                 175

Thr Lys Val Tyr Lys Asp Leu Leu Glu Asn Ser Met Leu Cys Ala Gly
            180                 185                 190

Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro
        195                 200                 205

Leu Val Cys Arg Gly Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Phe
```



```
    210                 215                 220

Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys
225                 230                 235                 240

Phe Thr Lys Trp Ile Asn Asp Thr Met Lys Lys His Arg
                245                 250
```

<210> 151
<211> 495
<212> PRT
<213> Homo sapiens

<400> 151

```
Met Val Thr Trp Leu Tyr Arg Phe Leu Pro Thr Ser Asn Met Ala Ala
1               5                   10                  15

Lys Leu Arg Ser Leu Leu Pro Pro Asp Leu Arg Leu Gln Phe Trp Leu
            20                  25                  30

His Ala Arg Leu Gln Lys Cys Phe Leu Ser Arg Gly Cys Gly Ser Tyr
        35                  40                  45

Cys Ala Gly Ala Lys Ala Ser Pro Leu Pro Gly Lys Met Ala Met Gly
    50                  55                  60

Leu Met Cys Gly Arg Arg Glu Leu Leu Arg Leu Leu Gln Ser Gly Arg
65                  70                  75                  80

Arg Val His Ser Val Ala Gly Pro Ser Gln Trp Leu Gly Lys Pro Leu
                85                  90                  95

Thr Thr Arg Leu Leu Phe Pro Val Ala Pro Cys Cys Cys Arg Pro His
            100                 105                 110

Tyr Leu Phe Leu Ala Ala Ser Gly Pro Arg Ser Leu Ser Thr Ser Ala
        115                 120                 125

Ile Ser Phe Ala Glu Val Gln Val Gln Ala Pro Pro Val Val Ala Ala
    130                 135                 140

Thr Pro Ser Pro Thr Ala Val Pro Glu Val Ala Ser Gly Glu Thr Ala
145                 150                 155                 160

Asp Val Val Gln Thr Ala Ala Glu Gln Ser Phe Ala Glu Leu Gly Leu
                165                 170                 175

Gly Ser Tyr Thr Pro Val Gly Leu Ile Gln Asn Leu Leu Glu Phe Met
            180                 185                 190

His Val Asp Leu Gly Leu Pro Trp Trp Gly Ala Ile Ala Ala Cys Thr
        195                 200                 205

Val Phe Ala Arg Cys Leu Ile Phe Pro Leu Ile Val Thr Gly Gln Arg
    210                 215                 220

Glu Ala Ala Arg Ile His Asn His Leu Pro Glu Ile Gln Lys Phe Ser
225                 230                 235                 240

Ser Arg Ile Arg Glu Ala Lys Leu Ala Gly Asp His Ile Glu Tyr Tyr
```

245 250 255

Lys Ala Ser Ser Glu Met Ala Leu Tyr Gln Lys Lys His Gly Ile Lys
260 265 270

Leu Tyr Lys Pro Leu Ile Leu Pro Val Thr Gln Ala Pro Ile Phe Ile
275 280 285

Ser Phe Phe Ile Ala Leu Arg Glu Met Ala Asn Leu Pro Val Pro Ser
290 295 300

Leu Gln Thr Gly Gly Leu Trp Trp Phe Gln Asp Leu Thr Val Ser Asp
305 310 315 320

Pro Ile Tyr Ile Leu Pro Leu Ala Val Thr Ala Thr Met Trp Ala Val
325 330 335

Leu Glu Leu Gly Ala Glu Thr Gly Val Gln Ser Ser Asp Leu Gln Trp
340 345 350

Met Arg Asn Val Ile Arg Met Met Pro Leu Ile Thr Leu Pro Ile Thr
355 360 365

Met His Phe Pro Thr Ala Val Phe Met Tyr Trp Leu Ser Ser Asn Leu
370 375 380

Phe Ser Leu Val Gln Val Ser Cys Leu Arg Ile Pro Ala Val Arg Thr
385 390 395 400

Val Leu Lys Ile Pro Gln Arg Val Val His Asp Leu Asp Lys Leu Pro
405 410 415

Pro Arg Glu Gly Phe Leu Glu Ser Phe Lys Lys Gly Trp Lys Asn Ala
420 425 430

Glu Met Thr Arg Gln Leu Arg Glu Arg Glu Gln Arg Met Arg Asn Gln
435 440 445

Leu Glu Leu Ala Ala Arg Gly Pro Leu Arg Gln Thr Phe Thr His Asn
450 455 460

Pro Leu Leu Gln Pro Gly Lys Asp Asn Pro Pro Asn Ile Pro Ser Ser
465 470 475 480

Ser Ser Lys Pro Lys Ser Lys Tyr Pro Trp His Asp Thr Leu Gly
485 490 495

<210> 152
<211> 351
<212> PRT
<213> Homo sapiens

<400> 152

Met Gly Asn Ala Ala Thr Ala Lys Lys Gly Ser Glu Val Glu Ser Val
1 5 10 15

Lys Glu Phe Leu Ala Lys Ala Lys Glu Asp Phe Leu Lys Lys Trp Glu
20 25 30

Asn Pro Thr Gln Asn Asn Ala Gly Leu Glu Asp Phe Glu Arg Lys Lys

35 40 45

Thr Leu Gly Thr Gly Ser Phe Gly Arg Val Met Leu Val Lys His Lys
50 55 60

Ala Thr Glu Gln Tyr Tyr Ala Met Lys Ile Leu Asp Lys Gln Lys Val
65 70 75 80

Val Lys Leu Lys Gln Ile Glu His Thr Leu Asn Glu Lys Arg Ile Leu
85 90 95

Gln Ala Val Asn Phe Pro Phe Leu Val Arg Leu Glu Tyr Ala Phe Lys
100 105 110

Asp Asn Ser Asn Leu Tyr Met Val Met Glu Tyr Val Pro Gly Gly Glu
115 120 125

Met Phe Ser His Leu Arg Arg Ile Gly Arg Phe Ser Glu Pro His Ala
130 135 140

Arg Phe Tyr Ala Ala Gln Ile Val Leu Thr Phe Glu Tyr Leu His Ser
145 150 155 160

Leu Asp Leu Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu Leu Ile Asp
165 170 175

His Gln Gly Tyr Ile Gln Val Thr Asp Phe Gly Phe Ala Lys Arg Val
180 185 190

Lys Gly Arg Thr Trp Thr Leu Cys Gly Thr Pro Glu Tyr Leu Ala Pro
195 200 205

Glu Ile Ile Leu Ser Lys Gly Tyr Asn Lys Ala Val Asp Trp Trp Ala
210 215 220

Leu Gly Val Leu Ile Tyr Glu Met Ala Ala Gly Tyr Pro Pro Phe Phe
225 230 235 240

Ala Asp Gln Pro Ile Gln Ile Tyr Glu Lys Ile Val Ser Gly Lys Val
245 250 255

Arg Phe Pro Ser His Phe Ser Ser Asp Leu Lys Asp Leu Leu Arg Asn
260 265 270

Leu Leu Gln Val Asp Leu Thr Lys Arg Phe Gly Asn Leu Lys Asn Gly
275 280 285

Val Ser Asp Ile Lys Thr His Lys Trp Phe Ala Thr Thr Asp Trp Ile
290 295 300

Ala Ile Tyr Gln Arg Lys Val Glu Ala Pro Phe Ile Pro Lys Phe Arg
305 310 315 320

Gly Ser Gly Asp Thr Ser Asn Phe Asp Asp Tyr Glu Glu Glu Asp Ile
325 330 335

Arg Val Ser Ile Thr Glu Lys Cys Ala Lys Glu Phe Gly Glu Phe
340 345 350

<210> 153
<211> 220
<212> PRT
<213> Homo sapiens

<400> 153

Met Val Phe Arg Arg Phe Val Glu Val Gly Arg Val Ala Tyr Val Ser
1 5 10 15

Phe Gly Pro His Ala Gly Lys Leu Val Ala Ile Val Asp Val Ile Asp
20 25 30

Gln Asn Arg Ala Leu Val Asp Gly Pro Cys Thr Gln Val Arg Arg Gln
35 40 45

Ala Met Pro Phe Lys Cys Met Gln Leu Thr Asp Phe Ile Leu Lys Phe
50 55 60

Leu His Ser Ala His Gln Lys Tyr Val Arg Gln Ala Trp Gln Lys Ala
65 70 75 80

Asp Ile Asn Thr Lys Trp Ala Ala Thr Arg Trp Ala Lys Lys Ile Glu
85 90 95

Ala Arg Glu Arg Lys Ala Lys Met Thr Asp Phe Asp Arg Phe Lys Val
100 105 110

Met Lys Ala Lys Lys Met Arg Asn Arg Ile Ile Lys Asn Glu Val Lys
115 120 125

Lys Leu Gln Lys Ala Ala Leu Leu Lys Ala Ser Pro Lys Lys Ala Pro
130 135 140

Gly Thr Lys Gly Thr Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala
145 150 155 160

Ala Ala Ala Ala Lys Val Pro Ala Lys Lys Ile Thr Ala Ala Ser Lys
165 170 175

Lys Ala Pro Ala Gln Lys Val Pro Ala Gln Lys Ala Thr Gly Gln Lys
180 185 190

Ala Ala Pro Ala Pro Lys Ala Gln Lys Gly Gln Lys Ala Pro Ala Gln
195 200 205

Lys Ala Pro Ala Pro Lys Ala Ser Gly Lys Lys Ala
210 215 220

<210> 154
<211> 492
<212> PRT
<213> Homo sapiens

<400> 154

Met Ala Pro Val Gly Val Glu Lys Lys Leu Leu Leu Gly Pro Asn Gly
1 5 10 15

Pro Ala Val Ala Ala Ala Gly Asp Leu Thr Ser Glu Glu Glu Glu Gly
20 25 30

Gln Ser Leu Trp Ser Ser Ile Leu Ser Glu Val Ser Thr Arg Ala Arg

35 40 45

Ser Lys Leu Pro Ser Gly Lys Asn Ile Leu Val Phe Gly Glu Asp Gly
50 55 60

Ser Gly Lys Thr Thr Leu Met Thr Lys Leu Gln Gly Ala Glu His Gly
65 70 75 80

Lys Lys Gly Arg Gly Leu Glu Tyr Leu Tyr Leu Ser Val His Asp Glu
85 90 95

Asp Arg Asp Asp His Thr Arg Cys Asn Val Trp Ile Leu Asp Gly Asp
100 105 110

Leu Tyr His Lys Gly Leu Leu Lys Phe Ala Val Ser Ala Glu Ser Leu
115 120 125

Pro Glu Thr Leu Val Ile Phe Val Ala Asp Met Ser Arg Pro Trp Thr
130 135 140

Val Met Glu Ser Leu Gln Lys Trp Ala Ser Val Leu Arg Glu His Ile
145 150 155 160

Asp Lys Met Lys Ile Pro Pro Glu Lys Met Arg Glu Leu Glu Arg Lys
165 170 175

Phe Val Lys Asp Phe Gln Asp Tyr Met Glu Pro Glu Glu Gly Cys Gln
180 185 190

Gly Ser Pro Gln Arg Arg Gly Pro Leu Thr Ser Gly Ser Asp Glu Glu
195 200 205

Asn Val Ala Leu Pro Leu Gly Asp Asn Val Leu Thr His Asn Leu Gly
210 215 220

Ile Pro Val Leu Val Val Cys Thr Lys Cys Asp Ala Val Ser Val Leu
225 230 235 240

Glu Lys Glu His Asp Tyr Arg Asp Glu His Leu Asp Phe Ile Gln Ser
245 250 255

His Leu Arg Arg Phe Cys Leu Gln Tyr Gly Ala Ala Leu Ile Tyr Thr
260 265 270

Ser Val Lys Glu Glu Lys Asn Leu Asp Leu Leu Tyr Lys Tyr Ile Val
275 280 285

His Lys Thr Tyr Gly Phe His Phe Thr Thr Pro Ala Leu Val Val Glu
290 295 300

Lys Asp Ala Val Phe Ile Pro Ala Gly Trp Asp Asn Glu Lys Lys Ile
305 310 315 320

Ala Ile Leu His Glu Asn Phe Thr Thr Val Lys Pro Glu Asp Ala Tyr
325 330 335

Glu Asp Phe Ile Val Lys Pro Pro Val Arg Lys Leu Val His Asp Lys
340 345 350

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Glu Leu Ala Ala Glu Asp Glu Gln Val Phe Leu Met Lys Gln Gln Ser
        355                 360                 365

Leu Leu Ala Lys Gln Pro Ala Thr Pro Thr Arg Ala Ser Glu Ser Pro
    370                 375                 380

Ala Arg Gly Pro Ser Gly Ser Pro Arg Thr Gln Gly Arg Gly Gly Pro
385                 390                 395                 400

Ala Ser Val Pro Ser Ser Ser Pro Gly Thr Ser Val Lys Lys Pro Asp
                405                 410                 415

Pro Asn Ile Lys Asn Asn Ala Ala Ser Glu Gly Val Leu Ala Ser Phe
            420                 425                 430

Phe Asn Ser Leu Leu Ser Lys Lys Thr Gly Ser Pro Gly Ser Pro Gly
        435                 440                 445

Ala Gly Gly Val Gln Ser Thr Ala Lys Lys Ser Gly Gln Lys Thr Val
    450                 455                 460

Leu Ser Asn Val Gln Glu Glu Leu Asp Arg Met Thr Arg Lys Pro Asp
465                 470                 475                 480

Ser Met Val Thr Asn Ser Ser Thr Glu Asn Glu Ala
                485                 490
```

<210> 155
<211> 2230
<212> PRT
<213> Homo sapiens

<400> 155

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Met Phe Lys Lys Leu Lys Gln Lys Ile Ser Glu Glu Gln Gln Gln Leu
1               5                   10                  15

Gln Gln Ala Leu Ala Pro Ala Gln Ala Ser Ser Asn Ser Ser Thr Pro
            20                  25                  30

Thr Arg Met Arg Ser Arg Thr Ser Ser Phe Thr Glu Gln Leu Asp Glu
        35                  40                  45

Gly Thr Pro Asn Arg Glu Ser Gly Asp Thr Gln Ser Phe Ala Gln Lys
    50                  55                  60

Leu Gln Leu Arg Val Pro Ser Val Glu Ser Leu Phe Arg Ser Pro Ile
65                  70                  75                  80

Lys Glu Ser Leu Phe Arg Ser Ser Ser Lys Glu Ser Leu Val Arg Thr
                85                  90                  95

Ser Ser Arg Glu Ser Leu Asn Arg Leu Asp Leu Asp Ser Ser Thr Ala
            100                 105                 110

Ser Phe Asp Pro Pro Ser Asp Met Asp Ser Glu Ala Glu Asp Leu Val
        115                 120                 125

Gly Asn Ser Asp Ser Leu Asn Lys Glu Gln Leu Ile Gln Arg Leu Arg
    130                 135                 140
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Arg Met Glu Arg Ser Leu Ser Ser Tyr Arg Gly Lys Tyr Ser Glu Leu
145                 150                 155                 160

Val Thr Ala Tyr Gln Met Leu Gln Arg Glu Lys Lys Lys Leu Gln Gly
                165                 170                 175

Ile Leu Ser Gln Ser Gln Asp Lys Ser Leu Arg Arg Ile Ala Glu Leu
            180                 185                 190

Arg Glu Glu Leu Gln Met Asp Gln Gln Ala Lys Lys His Leu Gln Glu
        195                 200                 205

Glu Phe Asp Ala Ser Leu Glu Glu Lys Asp Gln Tyr Ile Ser Val Leu
    210                 215                 220

Gln Thr Gln Val Ser Leu Leu Lys Gln Arg Leu Arg Asn Gly Pro Met
225                 230                 235                 240

Asn Val Asp Val Leu Lys Pro Leu Pro Gln Leu Glu Pro Gln Ala Glu
                245                 250                 255

Val Phe Thr Lys Glu Glu Asn Pro Glu Ser Asp Gly Glu Pro Val Val
            260                 265                 270

Glu Asp Gly Thr Ser Val Lys Thr Leu Glu Thr Leu Gln Gln Arg Val
        275                 280                 285

Lys Arg Gln Glu Asn Leu Leu Lys Arg Cys Lys Glu Thr Ile Gln Ser
    290                 295                 300

His Lys Glu Gln Cys Thr Leu Leu Thr Ser Glu Lys Glu Ala Leu Gln
305                 310                 315                 320

Glu Gln Leu Asp Glu Arg Leu Gln Glu Leu Glu Lys Ile Lys Asp Leu
                325                 330                 335

His Met Ala Glu Lys Thr Lys Leu Ile Thr Gln Leu Arg Asp Ala Lys
            340                 345                 350

Asn Leu Ile Glu Gln Leu Glu Gln Asp Lys Gly Met Val Ile Ala Glu
        355                 360                 365

Thr Lys Arg Gln Met His Glu Thr Leu Glu Met Lys Glu Glu Glu Ile
    370                 375                 380

Ala Gln Leu Arg Ser Arg Ile Lys Gln Met Thr Thr Gln Gly Glu Glu
385                 390                 395                 400

Leu Arg Glu Gln Lys Glu Lys Ser Glu Arg Ala Ala Phe Glu Glu Leu
                405                 410                 415

Glu Lys Ala Leu Ser Thr Ala Gln Lys Thr Glu Glu Ala Arg Arg Lys
            420                 425                 430

Leu Lys Ala Glu Met Asp Glu Gln Ile Lys Thr Ile Glu Lys Thr Ser
        435                 440                 445

Glu Glu Glu Arg Ile Ser Leu Gln Gln Glu Leu Ser Arg Val Lys Gln
    450                 455                 460
```

```
Glu Val Val Asp Val Met Lys Lys Ser Ser Glu Glu Gln Ile Ala Lys
465                 470                 475                 480

Leu Gln Lys Leu His Glu Lys Glu Leu Ala Arg Lys Glu Gln Glu Leu
                485                 490                 495

Thr Lys Lys Leu Gln Thr Arg Glu Arg Glu Phe Gln Glu Gln Met Lys
            500                 505                 510

Val Ala Leu Glu Lys Ser Gln Ser Glu Tyr Leu Lys Ile Ser Gln Glu
        515                 520                 525

Lys Glu Gln Gln Glu Ser Leu Ala Leu Glu Glu Leu Glu Leu Gln Lys
    530                 535                 540

Lys Ala Ile Leu Thr Glu Ser Glu Asn Lys Leu Arg Asp Leu Gln Gln
545                 550                 555                 560

Glu Ala Glu Thr Tyr Arg Thr Arg Ile Leu Glu Leu Glu Ser Ser Leu
                565                 570                 575

Glu Lys Ser Leu Gln Glu Asn Lys Asn Gln Ser Lys Asp Leu Ala Val
            580                 585                 590

His Leu Glu Ala Glu Lys Asn Lys His Asn Lys Glu Ile Thr Val Met
        595                 600                 605

Val Glu Lys His Lys Thr Glu Leu Glu Ser Leu Lys His Gln Gln Asp
    610                 615                 620

Ala Leu Trp Thr Glu Lys Leu Gln Val Leu Lys Gln Gln Tyr Gln Thr
625                 630                 635                 640

Glu Met Glu Lys Leu Arg Glu Lys Cys Glu Gln Glu Lys Glu Thr Leu
                645                 650                 655

Leu Lys Asp Lys Glu Ile Ile Phe Gln Ala His Ile Glu Glu Met Asn
            660                 665                 670

Glu Lys Thr Leu Glu Lys Leu Asp Val Lys Gln Thr Glu Leu Glu Ser
        675                 680                 685

Leu Ser Ser Glu Leu Ser Glu Val Leu Lys Ala Arg His Lys Leu Glu
    690                 695                 700

Glu Glu Leu Ser Val Leu Lys Asp Gln Thr Asp Lys Met Lys Gln Glu
705                 710                 715                 720

Leu Glu Ala Lys Met Asp Glu Gln Lys Asn His His Gln Gln Gln Val
                725                 730                 735

Asp Ser Ile Ile Lys Glu His Glu Val Ser Ile Gln Arg Thr Glu Lys
            740                 745                 750

Ala Leu Lys Asp Gln Ile Asn Gln Leu Glu Leu Leu Leu Lys Glu Arg
        755                 760                 765

Asp Lys His Leu Lys Glu His Gln Ala His Val Glu Asn Leu Glu Ala
    770                 775                 780
```



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Asp Ile Lys Arg Ser Glu Gly Glu Leu Gln Gln Ala Ser Ala Lys Leu
785                 790                 795                 800

Asp Val Phe Gln Ser Tyr Gln Ser Ala Thr His Glu Gln Thr Lys Ala
                805                 810                 815

Tyr Glu Glu Gln Leu Ala Gln Leu Gln Gln Lys Leu Leu Asp Leu Glu
            820                 825                 830

Thr Glu Arg Ile Leu Leu Thr Lys Gln Val Ala Glu Val Glu Ala Gln
        835                 840                 845

Lys Lys Asp Val Cys Thr Glu Leu Asp Ala His Lys Ile Gln Val Gln
    850                 855                 860

Asp Leu Met Gln Gln Leu Glu Lys Gln Asn Ser Glu Met Glu Gln Lys
865                 870                 875                 880

Val Lys Ser Leu Thr Gln Val Tyr Glu Ser Lys Leu Glu Asp Gly Asn
                885                 890                 895

Lys Glu Gln Glu Gln Thr Lys Gln Ile Leu Val Glu Lys Glu Asn Met
            900                 905                 910

Ile Leu Gln Met Arg Glu Gly Gln Lys Lys Glu Ile Glu Ile Leu Thr
        915                 920                 925

Gln Lys Leu Ser Ala Lys Glu Asp Ser Ile His Ile Leu Asn Glu Glu
    930                 935                 940

Tyr Glu Thr Lys Phe Lys Asn Gln Glu Lys Lys Met Glu Lys Val Lys
945                 950                 955                 960

Gln Lys Ala Lys Glu Met Gln Glu Thr Leu Lys Lys Lys Leu Leu Asp
                965                 970                 975

Gln Glu Ala Lys Leu Lys Lys Glu Leu Glu Asn Thr Ala Leu Glu Leu
            980                 985                 990

Ser Gln Lys Glu Lys Gln Phe Asn Ala Lys Met Leu Glu Met Ala Gln
        995                 1000                1005

Ala Asn Ser Ala Gly Ile Ser Asp Ala Val Ser Arg Leu Glu Thr
    1010                1015                1020

Asn Gln Lys Glu Gln Ile Glu Ser Leu Thr Glu Val His Arg Arg
    1025                1030                1035

Glu Leu Asn Asp Val Ile Ser Ile Trp Glu Lys Lys Leu Asn Gln
    1040                1045                1050

Gln Ala Glu Glu Leu Gln Glu Ile His Glu Ile Gln Leu Gln Glu
    1055                1060                1065

Lys Glu Gln Glu Val Ala Glu Leu Lys Gln Lys Ile Leu Leu Phe
    1070                1075                1080

Gly Cys Glu Lys Glu Glu Met Asn Lys Glu Ile Thr Trp Leu Lys
```

```
1085                1090                1095

Glu Glu Gly Val Lys Gln Asp Thr Thr Leu Asn Glu Leu Gln Glu
1100                1105                1110

Gln Leu Lys Gln Lys Ser Ala His Val Asn Ser Leu Ala Gln Asp
1115                1120                1125

Glu Thr Lys Leu Lys Ala His Leu Glu Lys Leu Glu Val Asp Leu
1130                1135                1140

Asn Lys Ser Leu Lys Glu Asn Thr Phe Leu Gln Glu Gln Leu Val
1145                1150                1155

Glu Leu Lys Met Leu Ala Glu Glu Asp Lys Arg Lys Val Ser Glu
1160                1165                1170

Leu Thr Ser Lys Leu Lys Thr Thr Asp Glu Glu Phe Gln Ser Leu
1175                1180                1185

Lys Ser Ser His Glu Lys Ser Asn Lys Ser Leu Glu Asp Lys Ser
1190                1195                1200

Leu Glu Phe Lys Lys Leu Ser Glu Glu Leu Ala Ile Gln Leu Asp
1205                1210                1215

Ile Cys Cys Lys Lys Thr Glu Ala Leu Leu Glu Ala Lys Thr Asn
1220                1225                1230

Glu Leu Ile Asn Ile Ser Ser Ser Lys Thr Asn Ala Ile Leu Ser
1235                1240                1245

Arg Ile Ser His Cys Gln His Arg Thr Thr Lys Val Lys Glu Ala
1250                1255                1260

Leu Leu Ile Lys Thr Cys Thr Val Ser Glu Leu Glu Ala Gln Leu
1265                1270                1275

Arg Gln Leu Thr Glu Glu Gln Asn Thr Leu Asn Ile Ser Phe Gln
1280                1285                1290

Gln Ala Thr His Gln Leu Glu Glu Lys Glu Asn Gln Ile Lys Ser
1295                1300                1305

Met Lys Ala Asp Ile Glu Ser Leu Val Thr Glu Lys Glu Ala Leu
1310                1315                1320

Gln Lys Glu Gly Gly Asn Gln Gln Gln Ala Ala Ser Glu Lys Glu
1325                1330                1335

Ser Cys Ile Thr Gln Leu Lys Lys Glu Leu Ser Glu Asn Ile Asn
1340                1345                1350

Ala Val Thr Leu Met Lys Glu Glu Leu Lys Glu Lys Lys Val Glu
1355                1360                1365

Ile Ser Ser Leu Ser Lys Gln Leu Thr Asp Leu Asn Val Gln Leu
1370                1375                1380
```



```
Gln Asn Ser Ile Ser Leu Ser Glu Lys Glu Ala Ala Ile Ser Ser
1385                1390                1395

Leu Arg Lys Gln Tyr Asp Glu Glu Lys Cys Glu Leu Leu Asp Gln
1400                1405                1410

Val Gln Asp Leu Ser Phe Lys Val Asp Thr Leu Ser Lys Glu Lys
1415                1420                1425

Ile Ser Ala Leu Glu Gln Val Asp Asp Trp Ser Asn Lys Phe Ser
1430                1435                1440

Glu Trp Lys Lys Lys Ala Gln Ser Arg Phe Thr Gln His Gln Asn
1445                1450                1455

Thr Val Lys Glu Leu Gln Ile Gln Leu Glu Leu Lys Ser Lys Glu
1460                1465                1470

Ala Tyr Glu Lys Asp Glu Gln Ile Asn Leu Leu Lys Glu Glu Leu
1475                1480                1485

Asp Gln Gln Asn Lys Arg Phe Asp Cys Leu Lys Gly Glu Met Glu
1490                1495                1500

Asp Asp Lys Ser Lys Met Glu Lys Lys Glu Ser Asn Leu Glu Thr
1505                1510                1515

Glu Leu Lys Ser Gln Thr Ala Arg Ile Met Glu Leu Glu Asp His
1520                1525                1530

Ile Thr Gln Lys Thr Ile Glu Ile Glu Ser Leu Asn Glu Val Leu
1535                1540                1545

Lys Asn Tyr Asn Gln Gln Lys Asp Ile Glu His Lys Glu Leu Val
1550                1555                1560

Gln Lys Leu Gln His Phe Gln Glu Leu Gly Glu Glu Lys Asp Asn
1565                1570                1575

Arg Val Lys Glu Ala Glu Glu Lys Ile Leu Thr Leu Glu Asn Gln
1580                1585                1590

Val Tyr Ser Met Lys Ala Glu Leu Glu Thr Lys Lys Lys Glu Leu
1595                1600                1605

Glu His Val Asn Leu Ser Val Lys Ser Lys Glu Glu Glu Leu Lys
1610                1615                1620

Ala Leu Glu Asp Arg Leu Glu Ser Glu Ser Ala Ala Lys Leu Ala
1625                1630                1635

Glu Leu Lys Arg Lys Ala Glu Gln Lys Ile Ala Ala Ile Lys Lys
1640                1645                1650

Gln Leu Leu Ser Gln Met Glu Glu Lys Glu Glu Gln Tyr Lys Lys
1655                1660                1665

Gly Thr Glu Ser His Leu Ser Glu Leu Asn Thr Lys Leu Gln Glu
1670                1675                1680
```

Arg Glu Arg Glu Val His Ile Leu Glu Glu Lys Leu Lys Ser Val
1685 1690 1695

Glu Ser Ser Gln Ser Glu Thr Leu Ile Val Pro Arg Ser Ala Lys
1700 1705 1710

Asn Val Ala Ala Tyr Thr Glu Gln Glu Glu Ala Asp Ser Gln Gly
1715 1720 1725

Cys Val Gln Lys Thr Tyr Glu Glu Lys Ile Ser Val Leu Gln Arg
1730 1735 1740

Asn Leu Thr Glu Lys Glu Lys Leu Leu Gln Arg Val Gly Gln Glu
1745 1750 1755

Lys Glu Glu Thr Val Ser Ser His Phe Glu Met Arg Cys Gln Tyr
1760 1765 1770

Gln Glu Arg Leu Ile Lys Leu Glu His Ala Glu Ala Lys Gln His
1775 1780 1785

Glu Asp Gln Ser Met Ile Gly His Leu Gln Glu Glu Leu Glu Glu
1790 1795 1800

Lys Asn Lys Lys Tyr Ser Leu Ile Val Ala Gln His Val Glu Lys
1805 1810 1815

Glu Gly Gly Lys Asn Asn Ile Gln Ala Lys Gln Asn Leu Glu Asn
1820 1825 1830

Val Phe Asp Asp Val Gln Lys Thr Leu Gln Glu Lys Glu Leu Thr
1835 1840 1845

Cys Gln Ile Leu Glu Gln Lys Ile Lys Glu Leu Asp Ser Cys Leu
1850 1855 1860

Val Arg Gln Lys Glu Val His Arg Val Glu Met Glu Glu Leu Thr
1865 1870 1875

Ser Lys Tyr Glu Lys Leu Gln Ala Leu Gln Gln Met Asp Gly Arg
1880 1885 1890

Asn Lys Pro Thr Glu Leu Leu Glu Glu Asn Thr Glu Glu Lys Ser
1895 1900 1905

Lys Ser His Leu Val Gln Pro Lys Leu Leu Ser Asn Met Glu Ala
1910 1915 1920

Gln His Asn Asp Leu Glu Phe Lys Leu Ala Gly Ala Glu Arg Glu
1925 1930 1935

Lys Gln Lys Leu Gly Lys Glu Ile Val Arg Leu Gln Lys Asp Leu
1940 1945 1950

Arg Met Leu Arg Lys Glu His Gln Gln Glu Leu Glu Ile Leu Lys
1955 1960 1965

Lys Glu Tyr Asp Gln Glu Arg Glu Glu Lys Ile Lys Gln Glu Gln
1970 1975 1980

Glu Asp Leu Glu Leu Lys His Asn Ser Thr Leu Lys Gln Leu Met
1985 1990 1995

Arg Glu Phe Asn Thr Gln Leu Ala Gln Lys Glu Gln Glu Leu Glu
2000 2005 2010

Met Thr Ile Lys Glu Thr Ile Asn Lys Ala Gln Glu Val Glu Ala
2015 2020 2025

Glu Leu Leu Glu Ser His Gln Glu Glu Thr Asn Gln Leu Leu Lys
2030 2035 2040

Lys Ile Ala Glu Lys Asp Asp Asp Leu Lys Arg Thr Ala Lys Arg
2045 2050 2055

Tyr Glu Glu Ile Leu Asp Ala Arg Glu Glu Glu Met Thr Ala Lys
2060 2065 2070

Val Arg Asp Leu Gln Thr Gln Leu Glu Glu Leu Gln Lys Lys Tyr
2075 2080 2085

Gln Gln Lys Leu Glu Gln Glu Glu Asn Pro Gly Asn Asp Asn Val
2090 2095 2100

Thr Ile Met Glu Leu Gln Thr Gln Leu Ala Gln Lys Thr Thr Leu
2105 2110 2115

Ile Ser Asp Ser Lys Leu Lys Glu Gln Glu Phe Arg Glu Gln Ile
2120 2125 2130

His Asn Leu Glu Asp Arg Leu Lys Lys Tyr Glu Lys Asn Val Tyr
2135 2140 2145

Ala Thr Thr Val Gly Thr Pro Tyr Lys Gly Gly Asn Leu Tyr His
2150 2155 2160

Thr Asp Val Ser Leu Phe Gly Glu Pro Thr Glu Phe Glu Tyr Leu
2165 2170 2175

Arg Lys Val Leu Phe Glu Tyr Met Met Gly Arg Glu Thr Lys Thr
2180 2185 2190

Met Ala Lys Val Ile Thr Thr Val Leu Lys Phe Pro Asp Asp Gln
2195 2200 2205

Thr Gln Lys Ile Leu Glu Arg Glu Asp Ala Arg Leu Met Phe Thr
2210 2215 2220

Ser Pro Arg Ser Gly Ile Phe
2225 2230

<210> 156
<211> 719
<212> PRT
<213> Homo sapiens

<400> 156

Glu Ile Met Glu Glu Leu Arg Ser Leu Asp Pro Arg Arg Gln Glu Leu
1 5 10 15

```
Leu Glu Ala Arg Phe Thr Gly Val Gly Val Ser Lys Gly Pro Leu Asn
            20                  25                  30

Ser Glu Ser Ser Asn Gln Ser Leu Cys Ser Val Gly Ser Leu Ser Asp
        35                  40                  45

Lys Glu Val Glu Thr Pro Glu Lys Lys Gln Asn Asp Gln Arg Asn Arg
    50                  55                  60

Lys Arg Lys Ala Glu Pro Tyr Glu Thr Ser Gln Gly Lys Gly Thr Pro
65                  70                  75                  80

Arg Gly His Lys Ile Ser Asp Tyr Phe Glu Arg Arg Val Glu Gln Pro
                85                  90                  95

Leu Tyr Gly Leu Asp Gly Ser Ala Ala Lys Glu Ala Thr Glu Glu Gln
            100                 105                 110

Ser Ala Leu Pro Thr Leu Met Ser Val Met Leu Ala Lys Pro Arg Leu
        115                 120                 125

Asp Pro Glu Gln Leu Ala Gln Arg Gly Ala Gly Leu Cys Phe Thr Phe
    130                 135                 140

Val Ser Ala Gln Gln Asn Ser Pro Ser Ser Thr Gly Ser Gly Asn Thr
145                 150                 155                 160

Glu His Ser Cys Ser Ser Gln Lys Gln Ile Ser Ile Gln His Arg Gln
                165                 170                 175

Thr Gln Ser Asp Leu Thr Ile Glu Lys Ile Ser Ala Leu Glu Asn Ser
            180                 185                 190

Lys Asn Ser Asp Leu Glu Lys Lys Glu Gly Arg Ile Asp Asp Leu Leu
        195                 200                 205

Arg Ala Asn Cys Asp Leu Arg Arg Gln Ile Asp Glu Gln Gln Lys Met
    210                 215                 220

Leu Glu Lys Tyr Lys Glu Arg Leu Asn Arg Cys Val Thr Met Ser Lys
225                 230                 235                 240

Lys Leu Leu Ile Glu Lys Ser Lys Gln Glu Lys Met Ala Cys Arg Asp
                245                 250                 255

Lys Ser Met Gln Asp Arg Leu Arg Leu Gly His Phe Thr Thr Val Arg
            260                 265                 270

His Gly Ala Ser Phe Thr Glu Gln Trp Thr Asp Gly Tyr Ala Phe Gln
        275                 280                 285

Asn Leu Ile Lys Gln Gln Glu Arg Ile Asn Ser Gln Arg Glu Glu Ile
    290                 295                 300

Glu Arg Gln Arg Lys Met Leu Ala Lys Arg Lys Pro Pro Ala Met Gly
305                 310                 315                 320

Gln Ala Pro Pro Ala Thr Asn Glu Gln Lys Gln Arg Lys Ser Lys Thr
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                325                 330                 335

Asn Gly Ala Glu Asn Glu Thr Leu Thr Leu Ala Glu Tyr His Glu Gln
            340                 345                 350

Glu Glu Ile Phe Lys Leu Arg Leu Gly His Leu Lys Lys Glu Glu Ala
        355                 360                 365

Glu Ile Gln Ala Glu Leu Glu Arg Leu Glu Arg Val Arg Asn Leu His
    370                 375                 380

Ile Arg Glu Leu Lys Arg Ile His Asn Glu Asp Asn Ser Gln Phe Lys
385                 390                 395                 400

Asp His Pro Thr Leu Asn Asp Arg Tyr Leu Leu Leu His Leu Leu Gly
                405                 410                 415

Arg Gly Gly Phe Ser Glu Val Tyr Lys Ala Phe Asp Leu Thr Glu Gln
            420                 425                 430

Arg Tyr Val Ala Val Lys Ile His Gln Leu Asn Lys Asn Trp Arg Asp
        435                 440                 445

Glu Lys Lys Glu Asn Tyr His Lys His Ala Cys Arg Glu Tyr Arg Ile
    450                 455                 460

His Lys Glu Leu Asp His Pro Arg Ile Val Lys Leu Tyr Asp Tyr Phe
465                 470                 475                 480

Ser Leu Asp Thr Asp Ser Phe Cys Thr Val Leu Glu Tyr Cys Glu Gly
                485                 490                 495

Asn Asp Leu Asp Phe Tyr Leu Lys Gln His Lys Leu Ile Ser Glu Lys
            500                 505                 510

Glu Ala Arg Ser Ile Ile Met Gln Ile Val Asn Ala Leu Lys Tyr Leu
        515                 520                 525

Asn Glu Ile Lys Pro Pro Ile Ile His Tyr Asp Leu Lys Pro Gly Asn
    530                 535                 540

Ile Leu Leu Val Asn Gly Thr Ala Cys Gly Glu Ile Lys Ile Thr Asp
545                 550                 555                 560

Phe Gly Leu Ser Lys Ile Met Asp Asp Asp Ser Tyr Asn Ser Val Asp
                565                 570                 575

Gly Met Glu Leu Thr Ser Gln Gly Ala Gly Thr Tyr Trp Tyr Leu Pro
            580                 585                 590

Pro Glu Cys Phe Val Val Gly Lys Glu Pro Pro Lys Ile Ser Asn Lys
        595                 600                 605

Val Asp Val Trp Ser Val Gly Val Ile Phe Tyr Gln Cys Leu Tyr Gly
    610                 615                 620

Arg Lys Pro Phe Gly His Asn Gln Ser Gln Gln Asp Ile Leu Gln Glu
625                 630                 635                 640
```

```
Asn Thr Ile Leu Lys Ala Thr Glu Val Gln Phe Pro Pro Lys Pro Val
                645                 650                 655

Val Thr Pro Glu Ala Lys Ala Phe Ile Arg Arg Cys Leu Ala Tyr Arg
            660                 665                 670

Lys Glu Asp Arg Ile Asp Val Gln Gln Leu Ala Cys Asp Pro Tyr Leu
        675                 680                 685

Leu Pro His Ile Arg Lys Ser Val Ser Thr Ser Ser Pro Ala Gly Ala
    690                 695                 700

Ala Ile Ala Ser Thr Ser Gly Ala Ser Asn Asn Ser Ser Ser Asn
705                 710                 715
```

<210> 157
<211> 1976
<212> PRT
<213> Homo sapiens

<400> 157

```
Met Ala Gln Arg Thr Gly Leu Glu Asp Pro Glu Arg Tyr Leu Phe Val
1               5                   10                  15

Asp Arg Ala Val Ile Tyr Asn Pro Ala Thr Gln Ala Asp Trp Thr Ala
            20                  25                  30

Lys Lys Leu Val Trp Ile Pro Ser Glu Arg His Gly Phe Glu Ala Ala
        35                  40                  45

Ser Ile Lys Glu Glu Arg Gly Asp Glu Val Met Val Glu Leu Ala Glu
    50                  55                  60

Asn Gly Lys Lys Ala Met Val Asn Lys Asp Asp Ile Gln Lys Met Asn
65                  70                  75                  80

Pro Pro Lys Phe Ser Lys Val Glu Asp Met Ala Glu Leu Thr Cys Leu
                85                  90                  95

Asn Glu Ala Ser Val Leu His Asn Leu Lys Asp Arg Tyr Tyr Ser Gly
            100                 105                 110

Leu Ile Tyr Thr Tyr Ser Gly Leu Phe Cys Val Val Ile Asn Pro Tyr
        115                 120                 125

Lys Asn Leu Pro Ile Tyr Ser Glu Asn Ile Ile Glu Met Tyr Arg Gly
    130                 135                 140

Lys Lys Arg His Glu Met Pro Pro His Ile Tyr Ala Ile Ser Glu Ser
145                 150                 155                 160

Ala Tyr Arg Cys Met Leu Gln Asp Arg Glu Asp Gln Ser Ile Leu Cys
                165                 170                 175

Thr Gly Glu Ser Gly Ala Gly Lys Thr Glu Asn Thr Lys Lys Val Ile
            180                 185                 190

Gln Tyr Leu Ala His Val Ala Ser Ser His Lys Gly Arg Lys Asp His
        195                 200                 205
```



```
Asn Ile Pro Gly Glu Leu Glu Arg Gln Leu Leu Gln Ala Asn Pro Ile
    210                 215                 220

Leu Glu Ser Phe Gly Asn Ala Lys Thr Val Lys Asn Asp Asn Ser Ser
225                 230                 235                 240

Arg Phe Gly Lys Phe Ile Arg Ile Asn Phe Asp Val Thr Gly Tyr Ile
                245                 250                 255

Val Gly Ala Asn Ile Glu Thr Tyr Leu Leu Glu Lys Ser Arg Ala Val
            260                 265                 270

Arg Gln Ala Lys Asp Glu Arg Thr Phe His Ile Phe Tyr Gln Leu Leu
        275                 280                 285

Ser Gly Ala Gly Glu His Leu Lys Ser Asp Leu Leu Leu Glu Gly Phe
    290                 295                 300

Asn Asn Tyr Arg Phe Leu Ser Asn Gly Tyr Ile Pro Ile Pro Gly Gln
305                 310                 315                 320

Gln Asp Lys Asp Asn Phe Gln Glu Thr Met Glu Ala Met His Ile Met
                325                 330                 335

Gly Phe Ser His Glu Glu Ile Leu Ser Met Leu Lys Val Val Ser Ser
            340                 345                 350

Val Leu Gln Phe Gly Asn Ile Ser Phe Lys Lys Glu Arg Asn Thr Asp
        355                 360                 365

Gln Ala Ser Met Pro Glu Asn Thr Val Ala Gln Lys Leu Cys His Leu
    370                 375                 380

Leu Gly Met Asn Val Met Glu Phe Thr Arg Ala Ile Leu Thr Pro Arg
385                 390                 395                 400

Ile Lys Val Gly Arg Asp Tyr Val Gln Lys Ala Gln Thr Lys Glu Gln
                405                 410                 415

Ala Asp Phe Ala Val Glu Ala Leu Ala Lys Ala Thr Tyr Glu Arg Leu
            420                 425                 430

Phe Arg Trp Leu Val His Arg Ile Asn Lys Ala Leu Asp Arg Thr Lys
        435                 440                 445

Arg Gln Gly Ala Ser Phe Ile Gly Ile Leu Asp Ile Ala Gly Phe Glu
    450                 455                 460

Ile Phe Glu Leu Asn Ser Phe Glu Gln Leu Cys Ile Asn Tyr Thr Asn
465                 470                 475                 480

Glu Lys Leu Gln Gln Leu Phe Asn His Thr Met Phe Ile Leu Glu Gln
                485                 490                 495

Glu Glu Tyr Gln Arg Glu Gly Ile Glu Trp Asn Phe Ile Asp Phe Gly
            500                 505                 510

Leu Asp Leu Gln Pro Cys Ile Asp Leu Ile Glu Arg Pro Ala Asn Pro
        515                 520                 525
```

```
Pro Gly Val Leu Ala Leu Leu Asp Glu Glu Cys Trp Phe Pro Lys Ala
    530                 535                 540

Thr Asp Lys Thr Phe Val Glu Lys Leu Val Gln Glu Gln Gly Ser His
545                 550                 555                 560

Ser Lys Phe Gln Lys Pro Arg Gln Leu Lys Asp Lys Ala Asp Phe Cys
                565                 570                 575

Ile Ile His Tyr Ala Gly Lys Val Asp Tyr Lys Ala Asp Glu Trp Leu
            580                 585                 590

Met Lys Asn Met Asp Pro Leu Asn Asp Asn Val Ala Thr Leu Leu His
        595                 600                 605

Gln Ser Ser Asp Arg Phe Val Ala Glu Leu Trp Lys Asp Val Asp Arg
    610                 615                 620

Ile Val Gly Leu Asp Gln Val Thr Gly Met Thr Glu Thr Ala Phe Gly
625                 630                 635                 640

Ser Ala Tyr Lys Thr Lys Lys Gly Met Phe Arg Thr Val Gly Gln Leu
                645                 650                 655

Tyr Lys Glu Ser Leu Thr Lys Leu Met Ala Thr Leu Arg Asn Thr Asn
            660                 665                 670

Pro Asn Phe Val Arg Cys Ile Ile Pro Asn His Glu Lys Arg Ala Gly
        675                 680                 685

Lys Leu Asp Pro His Leu Val Leu Asp Gln Leu Arg Cys Asn Gly Val
    690                 695                 700

Leu Glu Gly Ile Arg Ile Cys Arg Gln Gly Phe Pro Asn Arg Ile Val
705                 710                 715                 720

Phe Gln Glu Phe Arg Gln Arg Tyr Glu Ile Leu Thr Pro Asn Ala Ile
                725                 730                 735

Pro Lys Gly Phe Met Asp Gly Lys Gln Ala Cys Glu Arg Met Ile Arg
            740                 745                 750

Ala Leu Glu Leu Asp Pro Asn Leu Tyr Arg Ile Gly Gln Ser Lys Ile
        755                 760                 765

Phe Phe Arg Ala Gly Val Leu Ala His Leu Glu Glu Glu Arg Asp Leu
    770                 775                 780

Lys Ile Thr Asp Ile Ile Ile Phe Phe Gln Ala Val Cys Arg Gly Cys
785                 790                 795                 800

Leu Ala Arg Lys Ala Phe Ala Lys Lys Gln Gln Gln Leu Ser Ala Leu
                805                 810                 815

Lys Val Leu Gln Arg Asn Cys Ala Ala Tyr Leu Lys Leu Arg His Trp
            820                 825                 830

Gln Trp Trp Arg Val Phe Thr Lys Val Lys Pro Leu Leu Gln Val Thr
        835                 840                 845
```



```
Arg Gln Glu Glu Glu Leu Gln Ala Lys Asp Glu Glu Leu Leu Lys Val
    850                 855                 860

Lys Glu Lys Gln Thr Lys Val Glu Gly Glu Leu Glu Glu Met Glu Arg
865                 870                 875                 880

Lys His Gln Gln Leu Leu Glu Glu Lys Asn Ile Leu Ala Glu Gln Leu
                885                 890                 895

Gln Ala Glu Thr Glu Leu Phe Ala Glu Ala Glu Glu Met Arg Ala Arg
            900                 905                 910

Leu Ala Ala Lys Lys Gln Glu Leu Glu Glu Ile Leu His Asp Leu Glu
        915                 920                 925

Ser Arg Val Glu Glu Glu Glu Glu Arg Asn Gln Ile Leu Gln Asn Glu
    930                 935                 940

Lys Lys Lys Met Gln Ala His Ile Gln Asp Leu Glu Glu Gln Leu Asp
945                 950                 955                 960

Glu Glu Glu Gly Ala Arg Gln Lys Leu Gln Leu Glu Lys Val Thr Ala
                965                 970                 975

Glu Ala Lys Ile Lys Lys Met Glu Glu Glu Ile Leu Leu Leu Glu Asp
            980                 985                 990

Gln Asn Ser Lys Phe Ile Lys Glu  Lys Lys Leu Met Glu  Asp Arg Ile
        995                 1000                1005

Ala Glu  Cys Ser Ser Gln Leu  Ala Glu Glu Glu Glu  Lys Ala Lys
    1010                1015                1020

Asn Leu  Ala Lys Ile Arg Asn  Lys Gln Glu Val Met  Ile Ser Asp
    1025                1030                1035

Leu Glu  Glu Arg Leu Lys Lys  Glu Glu Lys Thr Arg  Gln Glu Leu
    1040                1045                1050

Glu Lys  Ala Lys Arg Lys Leu  Asp Gly Glu Thr Thr  Asp Leu Gln
    1055                1060                1065

Asp Gln  Ile Ala Glu Leu Gln  Ala Gln Ile Asp Glu  Leu Lys Leu
    1070                1075                1080

Gln Leu  Ala Lys Lys Glu Glu  Glu Leu Gln Gly Ala  Leu Ala Arg
    1085                1090                1095

Gly Asp  Asp Glu Thr Leu His  Lys Asn Asn Ala Leu  Lys Val Val
    1100                1105                1110

Arg Glu  Leu Gln Ala Gln Ile  Ala Glu Leu Gln Glu  Asp Phe Glu
    1115                1120                1125

Ser Glu  Lys Ala Ser Arg Asn  Lys Ala Glu Lys Gln  Lys Arg Asp
    1130                1135                1140

Leu Ser  Glu Glu Leu Glu Ala  Leu Lys Thr Glu Leu  Glu Asp Thr
```

1145 1150 1155

Leu Asp Thr Thr Ala Ala Gln Gln Glu Leu Arg Thr Lys Arg Glu
1160 1165 1170

Gln Glu Val Ala Glu Leu Lys Lys Ala Leu Glu Glu Glu Thr Lys
1175 1180 1185

Asn His Glu Ala Gln Ile Gln Asp Met Arg Gln Arg His Ala Thr
1190 1195 1200

Ala Leu Glu Glu Leu Ser Glu Gln Leu Glu Gln Ala Lys Arg Phe
1205 1210 1215

Lys Ala Asn Leu Glu Lys Asn Lys Gln Gly Leu Glu Thr Asp Asn
1220 1225 1230

Lys Glu Leu Ala Cys Glu Val Lys Val Leu Gln Gln Val Lys Ala
1235 1240 1245

Glu Ser Glu His Lys Arg Lys Lys Leu Asp Ala Gln Val Gln Glu
1250 1255 1260

Leu His Ala Lys Val Ser Glu Gly Asp Arg Leu Arg Val Glu Leu
1265 1270 1275

Ala Glu Lys Ala Ser Lys Leu Gln Asn Glu Leu Asp Asn Val Ser
1280 1285 1290

Thr Leu Leu Glu Glu Ala Glu Lys Lys Gly Ile Lys Phe Ala Lys
1295 1300 1305

Asp Ala Ala Ser Leu Glu Ser Gln Leu Gln Asp Thr Gln Glu Leu
1310 1315 1320

Leu Gln Glu Glu Thr Arg Gln Lys Leu Asn Leu Ser Ser Arg Ile
1325 1330 1335

Arg Gln Leu Glu Glu Glu Lys Asn Ser Leu Gln Glu Gln Gln Glu
1340 1345 1350

Glu Glu Glu Glu Ala Arg Lys Asn Leu Glu Lys Gln Val Leu Ala
1355 1360 1365

Leu Gln Ser Gln Leu Ala Asp Thr Lys Lys Lys Val Asp Asp Asp
1370 1375 1380

Leu Gly Thr Ile Glu Ser Leu Glu Glu Ala Lys Lys Lys Leu Leu
1385 1390 1395

Lys Asp Ala Glu Ala Leu Ser Gln Arg Leu Glu Glu Lys Ala Leu
1400 1405 1410

Ala Tyr Asp Lys Leu Glu Lys Thr Lys Asn Arg Leu Gln Gln Glu
1415 1420 1425

Leu Asp Asp Leu Thr Val Asp Leu Asp His Gln Arg Gln Val Ala
1430 1435 1440

Ser Asn Leu Glu Lys Lys Gln Lys Lys Phe Asp Gln Leu Leu Ala
1445 1450 1455

Glu Glu Lys Ser Ile Ser Ala Arg Tyr Ala Glu Glu Arg Asp Arg
1460 1465 1470

Ala Glu Ala Glu Ala Arg Glu Lys Glu Thr Lys Ala Leu Ser Leu
1475 1480 1485

Ala Arg Ala Leu Glu Glu Ala Leu Glu Ala Lys Glu Glu Phe Glu
1490 1495 1500

Arg Gln Asn Lys Gln Leu Arg Ala Asp Met Glu Asp Leu Met Ser
1505 1510 1515

Ser Lys Asp Asp Val Gly Lys Asn Val His Glu Leu Glu Lys Ser
1520 1525 1530

Lys Arg Ala Leu Glu Gln Gln Val Glu Glu Met Arg Thr Gln Leu
1535 1540 1545

Glu Glu Leu Glu Asp Glu Leu Gln Ala Thr Glu Asp Ala Lys Leu
1550 1555 1560

Arg Leu Glu Val Asn Met Gln Ala Met Lys Ala Gln Phe Glu Arg
1565 1570 1575

Asp Leu Gln Thr Arg Asp Glu Gln Asn Glu Glu Lys Lys Arg Leu
1580 1585 1590

Leu Ile Lys Gln Val Arg Glu Leu Glu Ala Glu Leu Glu Asp Glu
1595 1600 1605

Arg Lys Gln Arg Ala Leu Ala Val Ala Ser Lys Lys Lys Met Glu
1610 1615 1620

Ile Asp Leu Lys Asp Leu Glu Ala Gln Ile Glu Ala Ala Asn Lys
1625 1630 1635

Ala Arg Asp Glu Val Ile Lys Gln Leu Arg Lys Leu Gln Ala Gln
1640 1645 1650

Met Lys Asp Tyr Gln Arg Glu Leu Glu Glu Ala Arg Ala Ser Arg
1655 1660 1665

Asp Glu Ile Phe Ala Gln Ser Lys Glu Ser Glu Lys Lys Leu Lys
1670 1675 1680

Ser Leu Glu Ala Glu Ile Leu Gln Leu Gln Glu Glu Leu Ala Ser
1685 1690 1695

Ser Glu Arg Ala Arg Arg His Ala Glu Gln Glu Arg Asp Glu Leu
1700 1705 1710

Ala Asp Glu Ile Thr Asn Ser Ala Ser Gly Lys Ser Ala Leu Leu
1715 1720 1725

Asp Glu Lys Arg Arg Leu Glu Ala Arg Ile Ala Gln Leu Glu Glu
1730 1735 1740

```
Glu Leu  Glu Glu Glu Gln Ser  Asn Met Glu Leu Leu  Asn Asp Arg
    1745                1750                1755

Phe Arg  Lys Thr Thr Leu Gln  Val Asp Thr Leu Asn  Ala Glu Leu
    1760                1765                1770

Ala Ala  Glu Arg Ser Ala Ala  Gln Lys Ser Asp Asn  Ala Arg Gln
    1775                1780                1785

Gln Leu  Glu Arg Gln Asn Lys  Glu Leu Lys Ala Lys  Leu Gln Glu
    1790                1795                1800

Leu Glu  Gly Ala Val Lys Ser  Lys Phe Lys Ala Thr  Ile Ser Ala
    1805                1810                1815

Leu Glu  Ala Lys Ile Gly Gln  Leu Glu Glu Gln Leu  Glu Gln Glu
    1820                1825                1830

Ala Lys  Glu Arg Ala Ala Ala  Asn Lys Leu Val Arg  Arg Thr Glu
    1835                1840                1845

Lys Lys  Leu Lys Glu Ile Phe  Met Gln Val Glu Asp  Glu Arg Arg
    1850                1855                1860

His Ala  Asp Gln Tyr Lys Glu  Gln Met Glu Lys Ala  Asn Ala Arg
    1865                1870                1875

Met Lys  Gln Leu Lys Arg Gln  Leu Glu Glu Ala Glu  Glu Glu Ala
    1880                1885                1890

Thr Arg  Ala Asn Ala Ser Arg  Arg Lys Leu Gln Arg  Glu Leu Asp
    1895                1900                1905

Asp Ala  Thr Glu Ala Asn Glu  Gly Leu Ser Arg Glu  Val Ser Thr
    1910                1915                1920

Leu Lys  Asn Arg Leu Arg Arg  Gly Gly Pro Ile Ser  Phe Ser Ser
    1925                1930                1935

Ser Arg  Ser Gly Arg Arg Gln  Leu His Leu Glu Gly  Ala Ser Leu
    1940                1945                1950

Glu Leu  Ser Asp Asp Asp Thr  Glu Ser Lys Thr Ser  Asp Val Asn
    1955                1960                1965

Glu Thr  Gln Pro Pro Gln Ser  Glu
    1970                1975
```

<210> 158
<211> 1064
<212> PRT
<213> Homo sapiens

<400> 158

```
Met Lys Ile Ala Thr Val Ser Val Leu Leu Pro Leu Ala Leu Cys Leu
1               5                  10                  15

Ile Gln Asp Ala Ala Ser Lys Asn Glu Asp Gln Glu Met Cys His Glu
            20                  25                  30
```



```
Phe Gln Ala Phe Met Lys Asn Gly Lys Leu Phe Cys Pro Gln Asp Lys
        35                  40                  45

Lys Phe Phe Gln Ser Leu Asp Gly Ile Met Phe Ile Asn Lys Cys Ala
    50                  55                  60

Thr Cys Lys Met Ile Leu Glu Lys Glu Ala Lys Ser Gln Lys Arg Ala
65                  70                  75                  80

Arg His Leu Ala Arg Ala Pro Lys Ala Thr Ala Pro Thr Glu Leu Asn
                85                  90                  95

Cys Asp Asp Phe Lys Lys Gly Glu Arg Asp Gly Asp Phe Ile Cys Pro
            100                 105                 110

Asp Tyr Tyr Glu Ala Val Cys Gly Thr Asp Gly Lys Thr Tyr Asp Asn
        115                 120                 125

Arg Cys Ala Leu Cys Ala Glu Asn Ala Lys Thr Gly Ser Gln Ile Gly
    130                 135                 140

Val Lys Ser Glu Gly Glu Cys Lys Ser Ser Asn Pro Glu Gln Asp Val
145                 150                 155                 160

Cys Ser Ala Phe Arg Pro Phe Val Arg Asp Gly Arg Leu Gly Cys Thr
                165                 170                 175

Arg Glu Asn Asp Pro Val Leu Gly Pro Asp Gly Lys Thr His Gly Asn
            180                 185                 190

Lys Cys Ala Met Cys Ala Glu Leu Phe Leu Lys Glu Ala Glu Asn Ala
        195                 200                 205

Lys Arg Glu Gly Glu Thr Arg Ile Arg Arg Asn Ala Glu Lys Asp Phe
    210                 215                 220

Cys Lys Glu Tyr Glu Lys Gln Val Arg Asn Gly Arg Leu Phe Cys Thr
225                 230                 235                 240

Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly Arg Met His Gly Asn
                245                 250                 255

Lys Cys Ala Leu Cys Ala Glu Ile Phe Lys Arg Arg Phe Ser Glu Glu
            260                 265                 270

Asn Ser Lys Thr Asp Gln Asn Leu Gly Lys Ala Glu Glu Lys Thr Lys
        275                 280                 285

Val Lys Arg Glu Ile Val Lys Leu Cys Ser Gln Tyr Gln Asn Gln Ala
    290                 295                 300

Lys Asn Gly Ile Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Arg Gly
305                 310                 315                 320

Pro Asp Gly Lys Met His Gly Asn Leu Cys Ser Met Cys Gln Val Tyr
                325                 330                 335

Phe Gln Ala Glu Asn Glu Glu Lys Lys Lys Ala Glu Ala Arg Ala Arg
            340                 345                 350
```

```
Asn Lys Arg Glu Ser Gly Lys Ala Thr Ser Tyr Ala Glu Leu Cys Asn
        355                 360                 365

Glu Tyr Arg Lys Leu Val Arg Asn Gly Lys Leu Ala Cys Thr Arg Glu
    370                 375                 380

Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Val His Gly Asn Thr Cys
385                 390                 395                 400

Ser Met Cys Glu Val Phe Phe Gln Ala Glu Glu Glu Glu Lys Lys Lys
                405                 410                 415

Lys Glu Gly Glu Ser Arg Asn Lys Arg Gln Ser Lys Ser Thr Ala Ser
            420                 425                 430

Phe Glu Glu Leu Cys Ser Glu Tyr Arg Lys Ser Arg Lys Asn Gly Arg
        435                 440                 445

Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys
    450                 455                 460

Met His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln Gln Glu
465                 470                 475                 480

Glu Arg Ala Arg Ala Lys Ala Lys Arg Glu Ala Ala Lys Glu Ile Cys
                485                 490                 495

Ser Glu Phe Arg Asp Gln Val Arg Asn Gly Thr Leu Ile Cys Thr Arg
            500                 505                 510

Glu His Asn Pro Val Arg Gly Pro Asp Gly Lys Met His Gly Asn Lys
        515                 520                 525

Cys Ala Met Cys Ala Ser Val Phe Lys Leu Glu Glu Glu Glu Lys Lys
    530                 535                 540

Asn Asp Lys Glu Glu Lys Gly Lys Val Glu Ala Glu Lys Val Lys Arg
545                 550                 555                 560

Glu Ala Val Gln Glu Leu Cys Ser Glu Tyr Arg His Tyr Val Arg Asn
                565                 570                 575

Gly Arg Leu Pro Cys Thr Arg Glu Asn Asp Pro Ile Glu Gly Leu Asp
            580                 585                 590

Gly Lys Ile His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln
        595                 600                 605

Gln Glu Ala Lys Glu Lys Glu Arg Ala Glu Pro Arg Ala Lys Val Lys
    610                 615                 620

Arg Glu Ala Glu Lys Glu Thr Cys Asp Glu Phe Arg Arg Leu Leu Gln
625                 630                 635                 640

Asn Gly Lys Leu Phe Cys Thr Arg Glu Asn Asp Pro Val Arg Gly Pro
                645                 650                 655

Asp Gly Lys Thr His Gly Asn Lys Cys Ala Met Cys Lys Ala Val Phe
```



```
            660                 665                 670

Gln Lys Glu Asn Glu Glu Arg Lys Arg Lys Glu Glu Glu Asp Gln Arg
        675                 680                 685

Asn Ala Ala Gly His Gly Ser Ser Gly Gly Gly Gly Gly Asn Thr Gln
    690                 695                 700

Asp Glu Cys Ala Glu Tyr Gln Glu Gln Met Lys Asn Gly Arg Leu Ser
705                 710                 715                 720

Cys Thr Arg Glu Ser Asp Pro Val Arg Asp Ala Asp Gly Lys Ser Tyr
                725                 730                 735

Asn Asn Gln Cys Thr Met Cys Lys Ala Lys Leu Glu Arg Glu Ala Glu
            740                 745                 750

Arg Lys Asn Glu Tyr Ser Arg Ser Arg Ser Asn Gly Thr Gly Ser Glu
        755                 760                 765

Ser Gly Lys Asp Thr Cys Asp Glu Phe Arg Ser Gln Met Lys Asn Gly
    770                 775                 780

Lys Leu Ile Cys Thr Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly
785                 790                 795                 800

Lys Thr His Gly Asn Lys Cys Thr Met Cys Lys Glu Lys Leu Glu Arg
                805                 810                 815

Glu Ala Ala Glu Lys Lys Lys Lys Glu Asp Glu Asp Arg Ser Asn Thr
            820                 825                 830

Gly Glu Arg Ser Asn Thr Gly Glu Arg Ser Asn Asp Lys Glu Asp Leu
        835                 840                 845

Cys Arg Glu Phe Arg Ser Met Gln Arg Asn Gly Lys Leu Ile Cys Thr
    850                 855                 860

Arg Glu Asn Asn Pro Val Arg Gly Pro Tyr Gly Lys Met His Ile Asn
865                 870                 875                 880

Lys Cys Ala Met Cys Gln Ser Ile Phe Asp Arg Glu Ala Asn Glu Arg
                885                 890                 895

Lys Lys Lys Asp Glu Glu Lys Ser Ser Ser Lys Pro Ser Asn Asn Ala
            900                 905                 910

Lys Asp Glu Cys Ser Glu Phe Arg Asn Tyr Ile Arg Asn Asn Glu Leu
        915                 920                 925

Ile Cys Pro Arg Glu Asn Asp Pro Val His Gly Ala Asp Gly Lys Phe
    930                 935                 940

Tyr Thr Asn Lys Cys Tyr Met Cys Arg Ala Val Phe Leu Thr Glu Ala
945                 950                 955                 960

Leu Glu Arg Ala Lys Leu Gln Glu Lys Pro Ser His Val Arg Ala Ser
                965                 970                 975
```

Gln Glu Glu Asp Ser Pro Asp Ser Phe Ser Ser Leu Asp Ser Glu Met
980 985 990

Cys Lys Asp Tyr Arg Val Leu Pro Arg Ile Gly Tyr Leu Cys Pro Lys
995 1000 1005

Asp Leu Lys Pro Val Cys Gly Asp Asp Gly Gln Thr Tyr Asn Asn
1010 1015 1020

Pro Cys Met Leu Cys His Glu Asn Leu Ile Arg Gln Thr Asn Thr
1025 1030 1035

His Ile Arg Ser Thr Gly Lys Cys Glu Glu Ser Ser Thr Pro Gly
1040 1045 1050

Thr Thr Ala Ala Ser Met Pro Pro Ser Asp Glu
1055 1060

<210> 159
<211> 125
<212> PRT
<213> Homo sapiens

<400> 159

Met His Lys Glu Glu His Glu Val Ala Val Leu Gly Ala Pro Pro Ser
1 5 10 15

Thr Ile Leu Pro Arg Ser Thr Val Ile Asn Ile His Ser Glu Thr Ser
20 25 30

Val Pro Asp His Val Val Trp Ser Leu Phe Asn Thr Leu Phe Leu Asn
35 40 45

Trp Cys Cys Leu Gly Phe Ile Ala Phe Ala Tyr Ser Val Lys Ser Arg
50 55 60

Asp Arg Lys Met Val Gly Asp Val Thr Gly Ala Gln Ala Tyr Ala Ser
65 70 75 80

Thr Ala Lys Cys Leu Asn Ile Trp Ala Leu Ile Leu Gly Ile Leu Met
85 90 95

Thr Ile Gly Phe Ile Leu Leu Leu Val Phe Gly Ser Val Thr Val Tyr
100 105 110

His Ile Met Leu Gln Ile Ile Gln Glu Lys Arg Gly Tyr
115 120 125

<210> 160
<211> 400
<212> PRT
<213> Homo sapiens

<400> 160

Met Met Asp Leu Arg Asn Thr Pro Ala Lys Ser Leu Asp Lys Phe Ile
1 5 10 15

Glu Asp Tyr Leu Leu Pro Asp Thr Cys Phe Arg Met Gln Ile Asp His
20 25 30

Ala Ile Asp Ile Ile Cys Gly Phe Leu Lys Glu Arg Cys Phe Arg Gly

35 40 45

Ser Ser Tyr Pro Val Cys Val Ser Lys Val Val Lys Gly Gly Ser Ser
50 55 60

Gly Lys Gly Thr Thr Leu Arg Gly Arg Ser Asp Ala Asp Leu Val Val
65 70 75 80

Phe Leu Ser Pro Leu Thr Thr Phe Gln Asp Gln Leu Asn Arg Arg Gly
85 90 95

Glu Phe Ile Gln Glu Ile Arg Arg Gln Leu Glu Ala Cys Gln Arg Glu
100 105 110

Arg Ala Leu Ser Val Lys Phe Glu Val Gln Ala Pro Arg Trp Gly Asn
115 120 125

Pro Arg Ala Leu Ser Phe Val Leu Ser Ser Leu Gln Leu Gly Glu Gly
130 135 140

Val Glu Phe Asp Val Leu Pro Ala Phe Asp Ala Leu Gly Gln Leu Thr
145 150 155 160

Gly Ser Tyr Lys Pro Asn Pro Gln Ile Tyr Val Lys Leu Ile Glu Glu
165 170 175

Cys Thr Asp Leu Gln Lys Glu Gly Glu Phe Ser Thr Cys Phe Thr Glu
180 185 190

Leu Gln Arg Asp Phe Leu Lys Gln Arg Pro Thr Lys Leu Lys Ser Leu
195 200 205

Ile Arg Leu Val Lys His Trp Tyr Gln Asn Cys Lys Lys Lys Leu Gly
210 215 220

Lys Leu Pro Pro Gln Tyr Ala Leu Glu Leu Leu Thr Val Tyr Ala Trp
225 230 235 240

Glu Arg Gly Ser Met Lys Thr His Phe Asn Thr Ala Gln Gly Phe Arg
245 250 255

Thr Val Leu Glu Leu Val Ile Asn Tyr Gln Gln Leu Cys Ile Tyr Trp
260 265 270

Thr Lys Tyr Tyr Asp Phe Lys Asn Pro Ile Ile Glu Lys Tyr Leu Arg
275 280 285

Arg Gln Leu Thr Lys Pro Arg Pro Val Ile Leu Asp Pro Ala Asp Pro
290 295 300

Thr Gly Asn Leu Gly Gly Gly Asp Pro Lys Gly Trp Arg Gln Leu Ala
305 310 315 320

Gln Glu Ala Glu Ala Trp Leu Asn Tyr Pro Cys Phe Lys Asn Trp Asp
325 330 335

Gly Ser Pro Val Ser Ser Trp Ile Leu Leu Ala Glu Ser Asn Ser Thr
340 345 350

```
Asp Asp Glu Thr Asp Asp Pro Arg Thr Tyr Gln Lys Tyr Gly Tyr Ile
        355                 360                 365

Gly Thr His Glu Tyr Pro His Phe Ser His Arg Pro Ser Thr Leu Gln
    370                 375                 380

Ala Ala Ser Thr Pro Gln Ala Glu Glu Asp Trp Thr Cys Thr Ile Leu
385                 390                 395                 400
```

<210> 161
<211> 370
<212> PRT
<213> Homo sapiens

<400> 161

```
Met Glu Asn Gln Val Leu Thr Pro His Val Tyr Trp Ala Gln Arg His
1               5                   10                  15

Arg Glu Leu Tyr Leu Arg Val Glu Leu Ser Asp Val Gln Asn Pro Ala
            20                  25                  30

Ile Ser Ile Thr Glu Asn Val Leu His Phe Lys Ala Gln Gly His Gly
        35                  40                  45

Ala Lys Gly Asp Asn Val Tyr Glu Phe His Leu Glu Phe Leu Asp Leu
    50                  55                  60

Val Lys Pro Glu Pro Val Tyr Lys Leu Thr Gln Arg Gln Val Asn Ile
65                  70                  75                  80

Thr Val Gln Lys Lys Val Ser Gln Trp Trp Glu Arg Leu Thr Lys Gln
                85                  90                  95

Glu Lys Arg Pro Leu Phe Leu Ala Pro Asp Phe Asp Arg Trp Leu Asp
            100                 105                 110

Glu Ser Asp Ala Glu Met Glu Leu Arg Ala Lys Glu Glu Glu Arg Leu
        115                 120                 125

Asn Lys Leu Arg Leu Glu Ser Glu Gly Ser Pro Glu Thr Leu Thr Asn
    130                 135                 140

Leu Arg Lys Gly Tyr Leu Phe Met Tyr Asn Leu Val Gln Phe Leu Gly
145                 150                 155                 160

Phe Ser Trp Ile Phe Val Asn Leu Thr Val Arg Phe Cys Ile Leu Gly
                165                 170                 175

Lys Glu Ser Phe Tyr Asp Thr Phe His Thr Val Ala Asp Met Met Tyr
            180                 185                 190

Phe Cys Gln Met Leu Ala Val Val Glu Thr Ile Asn Ala Ala Ile Gly
        195                 200                 205

Val Thr Thr Ser Pro Val Leu Pro Ser Leu Ile Gln Leu Leu Gly Arg
    210                 215                 220

Asn Phe Ile Leu Phe Ile Ile Phe Gly Thr Met Glu Glu Met Gln Asn
225                 230                 235                 240
```



```
Lys Ala Val Val Phe Phe Val Phe Tyr Leu Trp Ser Ala Ile Glu Ile
                245                 250                 255

Phe Arg Tyr Ser Phe Tyr Met Leu Thr Cys Ile Asp Met Asp Trp Lys
            260                 265                 270

Val Leu Thr Trp Leu Arg Tyr Thr Leu Trp Ile Pro Leu Tyr Pro Leu
        275                 280                 285

Gly Cys Leu Ala Glu Ala Val Ser Val Ile Gln Ser Ile Pro Ile Phe
    290                 295                 300

Asn Glu Thr Gly Arg Phe Ser Phe Thr Leu Pro Tyr Pro Val Lys Ile
305                 310                 315                 320

Lys Val Arg Phe Ser Phe Phe Leu Gln Ile Tyr Leu Ile Met Ile Phe
                325                 330                 335

Leu Gly Leu Tyr Ile Asn Phe Arg His Leu Tyr Lys Gln Arg Arg Leu
            340                 345                 350

Lys Met Arg Ala Gly Ala Val Ala His Ala Cys Asp Pro Ser Ala Leu
        355                 360                 365

Gly Gly
    370
```

<210> 162
<211> 372
<212> PRT
<213> Homo sapiens

<400> 162

```
Met Leu Asp Gly Leu Gly Val Val Ala Ile Ser Ile Phe Gly Ile Gln
1               5                   10                  15

Leu Lys Thr Glu Gly Ser Leu Arg Thr Ala Val Pro Gly Ile Pro Thr
            20                  25                  30

Gln Ser Ala Phe Asn Lys Cys Leu Gln Arg Tyr Ile Gly Ala Leu Gly
        35                  40                  45

Ala Arg Val Ile Cys Asp Asn Ile Pro Gly Leu Val Ser Arg Gln Arg
    50                  55                  60

Gln Leu Cys Gln Arg Tyr Pro Asp Ile Met Arg Ser Val Gly Glu Gly
65                  70                  75                  80

Ala Arg Glu Trp Ile Arg Glu Cys Gln His Gln Phe Arg His His Arg
                85                  90                  95

Trp Asn Cys Thr Thr Leu Asp Arg Asp His Thr Val Phe Gly Arg Val
            100                 105                 110

Met Leu Arg Ser Ser Arg Glu Ala Ala Phe Val Tyr Ala Ile Ser Ser
        115                 120                 125

Ala Gly Val Ile His Ala Ile Thr Arg Ala Cys Ser Gln Gly Glu Leu
    130                 135                 140
```

```
Ser Val Cys Ser Cys Asp Pro Tyr Thr Arg Gly Arg His His Asp Gln
145                 150                 155                 160

Arg Gly Thr Phe Asp Trp Gly Gly Cys Ser Asp Asn Ile His Tyr Gly
                165                 170                 175

Val Arg Phe Ala Lys Ala Phe Val Asp Ala Lys Glu Lys Arg Leu Lys
            180                 185                 190

Asp Ala Arg Ala Leu Met Asn Leu His Asn Asn Arg Cys Gly Arg Thr
        195                 200                 205

Ala Val Arg Arg Phe Val Lys Leu Glu Cys Lys Cys His Gly Val Ser
    210                 215                 220

Gly Ser Cys Thr Leu Arg Thr Cys Trp Arg Ala Leu Ser Asp Phe Arg
225                 230                 235                 240

Arg Thr Gly Asp Tyr Leu Arg Arg Arg Tyr Asp Gly Ala Val Gln Val
                245                 250                 255

Met Ala Thr Gln Asp Gly Ala Asn Phe Thr Ala Ala Arg Gln Gly Tyr
            260                 265                 270

Arg Arg Ala Thr Arg Ser Asp Leu Val Tyr Phe Asp Asn Ser Pro Asp
        275                 280                 285

Tyr Cys Val Leu Asp Lys Ala Ala Gly Ser Leu Gly Thr Ala Gly Arg
    290                 295                 300

Val Cys Ser Lys Thr Ser Lys Gly Thr Asp Gly Cys Glu Ile Met Cys
305                 310                 315                 320

Cys Gly Arg Gly Tyr Asp Thr Thr Arg Val Thr Arg Val Thr Gln Cys
                325                 330                 335

Glu Cys Lys Phe His Trp Cys Cys Ala Val Arg Cys Lys Glu Cys Arg
            340                 345                 350

Asn Thr Val Asp Val His Thr Cys Lys Ala Pro Lys Lys Ala Glu Trp
        355                 360                 365

Leu Asp Gln Thr
    370
```

<210> 163
<211> 249
<212> PRT
<213> Homo sapiens

<400> 163

```
Met Lys Leu Asn Ile Ser Phe Pro Ala Thr Gly Cys Gln Lys Leu Ile
1               5                   10                  15

Glu Val Asp Asp Glu Arg Thr Leu Arg Thr Phe Tyr Glu Lys Arg Met
            20                  25                  30

Ala Thr Glu Val Ala Ala Asp Ala Leu Gly Glu Glu Trp Lys Gly Tyr
        35                  40                  45
```



```
Val Val Arg Ile Ser Gly Gly Asn Asp Lys Gln Gly Phe Pro Met Lys
    50                  55                  60

Gln Gly Val Leu Thr His Gly Arg Val Arg Leu Leu Leu Ser Lys Gly
65                  70                  75                  80

His Ser Cys Tyr Arg Pro Arg Arg Thr Gly Glu Arg Lys Arg Lys Ser
                85                  90                  95

Val Arg Gly Cys Ile Val Asp Ala Asn Leu Ser Val Leu Asn Leu Val
            100                 105                 110

Ile Val Lys Lys Gly Glu Lys Asp Ile Pro Gly Leu Thr Asp Thr Thr
        115                 120                 125

Val Pro Arg Arg Leu Gly Pro Lys Arg Ala Ser Arg Ile Arg Lys Arg
    130                 135                 140

Phe Asn Leu Ser Lys Glu Asp Asp Val Arg Gln Tyr Val Val Arg Lys
145                 150                 155                 160

Pro Leu Asn Lys Glu Gly Lys Lys Pro Arg Thr Lys Ala Pro Lys Ile
                165                 170                 175

Gln Arg Leu Val Thr Pro Arg Val Leu Gln His Lys Arg Arg Arg Ile
            180                 185                 190

Ala Leu Lys Gln Gln Arg Thr Lys Lys Asn Lys Glu Glu Ala Ala Glu
        195                 200                 205

Tyr Ala Lys Leu Leu Ala Lys Arg Met Lys Glu Ala Lys Glu Lys Arg
    210                 215                 220

Gln Glu Gln Ile Ala Lys Arg Arg Arg Leu Ser Ser Leu Arg Ala Ser
225                 230                 235                 240

Thr Ser Lys Ser Glu Ser Ser Gln Lys
                245
```

<210> 164
<211> 469
<212> PRT
<213> Homo sapiens

<400> 164

```
Met His Ser Phe Pro Pro Leu Leu Leu Leu Leu Phe Trp Gly Val Val
1               5                   10                  15

Ser His Ser Phe Pro Ala Thr Leu Glu Thr Gln Glu Gln Asp Val Asp
            20                  25                  30

Leu Val Gln Lys Tyr Leu Glu Lys Tyr Tyr Asn Leu Lys Asn Asp Gly
        35                  40                  45

Arg Gln Val Glu Lys Arg Arg Asn Ser Gly Pro Val Val Glu Lys Leu
    50                  55                  60

Lys Gln Met Gln Glu Phe Phe Gly Leu Lys Val Thr Gly Lys Pro Asp
65                  70                  75                  80
```

```
Ala Glu Thr Leu Lys Val Met Lys Gln Pro Arg Cys Gly Val Pro Asp
                85                  90                  95

Val Ala Gln Phe Val Leu Thr Glu Gly Asn Pro Arg Trp Glu Gln Thr
            100                 105                 110

His Leu Thr Tyr Arg Ile Glu Asn Tyr Thr Pro Asp Leu Pro Arg Ala
        115                 120                 125

Asp Val Asp His Ala Ile Glu Lys Ala Phe Gln Leu Trp Ser Asn Val
    130                 135                 140

Thr Pro Leu Thr Phe Thr Lys Val Ser Glu Gly Gln Ala Asp Ile Met
145                 150                 155                 160

Ile Ser Phe Val Arg Gly Asp His Arg Asp Asn Ser Pro Phe Asp Gly
                165                 170                 175

Pro Gly Gly Asn Leu Ala His Ala Phe Gln Pro Gly Pro Gly Ile Gly
            180                 185                 190

Gly Asp Ala His Phe Asp Glu Asp Glu Arg Trp Thr Asn Asn Phe Arg
        195                 200                 205

Glu Tyr Asn Leu His Arg Val Ala Ala His Glu Leu Gly His Ser Leu
    210                 215                 220

Gly Leu Ser His Ser Thr Asp Ile Gly Ala Leu Met Tyr Pro Ser Tyr
225                 230                 235                 240

Thr Phe Ser Gly Asp Val Gln Leu Ala Gln Asp Asp Ile Asp Gly Ile
                245                 250                 255

Gln Ala Ile Tyr Gly Arg Ser Gln Asn Pro Val Gln Pro Ile Gly Pro
            260                 265                 270

Gln Thr Pro Lys Ala Cys Asp Ser Lys Leu Thr Phe Asp Ala Ile Thr
        275                 280                 285

Thr Ile Arg Gly Glu Val Met Phe Phe Lys Asp Arg Phe Tyr Met Arg
    290                 295                 300

Thr Asn Pro Phe Tyr Pro Glu Val Glu Leu Asn Phe Ile Ser Val Phe
305                 310                 315                 320

Trp Pro Gln Leu Pro Asn Gly Leu Glu Ala Ala Tyr Glu Phe Ala Asp
                325                 330                 335

Arg Asp Glu Val Arg Phe Phe Lys Gly Asn Lys Tyr Trp Ala Val Gln
            340                 345                 350

Gly Gln Asn Val Leu His Gly Tyr Pro Lys Asp Ile Tyr Ser Ser Phe
        355                 360                 365

Gly Phe Pro Arg Thr Val Lys His Ile Asp Ala Ala Leu Ser Glu Glu
    370                 375                 380

Asn Thr Gly Lys Thr Tyr Phe Phe Val Ala Asn Lys Tyr Trp Arg Tyr
385                 390                 395                 400
```



```
Asp Glu Tyr Lys Arg Ser Met Asp Pro Gly Tyr Pro Lys Met Ile Ala
                405                 410                 415

His Asp Phe Pro Gly Ile Gly His Lys Val Asp Ala Val Phe Met Lys
            420                 425                 430

Asp Gly Phe Phe Tyr Phe Phe His Gly Thr Arg Gln Tyr Lys Phe Asp
        435                 440                 445

Pro Lys Thr Lys Arg Ile Leu Thr Leu Gln Lys Ala Asn Ser Trp Phe
    450                 455                 460

Asn Cys Arg Lys Asn
465
```

<210> 165
<211> 156
<212> PRT
<213> Homo sapiens

<400> 165

```
Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu
1               5                   10                  15

Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp
            20                  25                  30

Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys
        35                  40                  45

Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu
    50                  55                  60

Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Ala Lys Lys Arg
65                  70                  75                  80

Lys Lys Lys Ser Tyr Thr Thr Pro Lys Lys Asn Lys His Lys Arg Lys
                85                  90                  95

Lys Val Lys Leu Ala Val Leu Lys Tyr Tyr Lys Val Asp Glu Asn Gly
            100                 105                 110

Lys Ile Ser Arg Leu Arg Arg Glu Cys Pro Ser Asp Glu Cys Gly Ala
        115                 120                 125

Gly Val Phe Met Ala Ser His Phe Asp Arg His Tyr Cys Gly Lys Cys
    130                 135                 140

Cys Leu Thr Tyr Cys Phe Asn Lys Pro Glu Asp Lys
145                 150                 155
```

<210> 166
<211> 783
<212> PRT
<213> Homo sapiens

<400> 166

```
Met Ala Lys Tyr Asn Thr Gly Gly Asn Pro Thr Glu Asp Val Ser Val
1               5                   10                  15
```

```
Asn Ser Arg Pro Phe Arg Val Thr Gly Pro Asn Ser Ser Ser Gly Ile
            20                  25                  30

Gln Ala Arg Lys Asn Leu Phe Asn Asn Gln Gly Asn Ala Ser Pro Pro
        35                  40                  45

Ala Gly Pro Ser Asn Val Pro Lys Phe Gly Ser Pro Lys Pro Pro Val
    50                  55                  60

Ala Val Lys Pro Ser Ser Glu Glu Lys Pro Asp Lys Glu Pro Lys Pro
65                  70                  75                  80

Pro Phe Leu Lys Pro Thr Gly Ala Gly Gln Arg Phe Gly Thr Pro Ala
                85                  90                  95

Ser Leu Thr Thr Arg Asp Pro Glu Ala Lys Val Gly Phe Leu Lys Pro
            100                 105                 110

Val Gly Pro Lys Pro Ile Asn Leu Pro Lys Glu Asp Ser Lys Pro Thr
        115                 120                 125

Phe Pro Trp Pro Pro Gly Asn Lys Pro Ser Leu His Ser Val Asn Gln
    130                 135                 140

Asp His Asp Leu Lys Pro Leu Gly Pro Lys Ser Gly Pro Thr Pro Pro
145                 150                 155                 160

Thr Ser Glu Asn Glu Gln Lys Gln Ala Phe Pro Lys Leu Thr Gly Val
                165                 170                 175

Lys Gly Lys Phe Met Ser Ala Ser Gln Asp Leu Glu Pro Lys Pro Leu
            180                 185                 190

Phe Pro Lys Pro Ala Phe Gly Gln Lys Pro Pro Leu Ser Thr Glu Asn
        195                 200                 205

Ser His Glu Asp Glu Ser Pro Met Lys Asn Val Ser Ser Ser Lys Gly
    210                 215                 220

Ser Pro Ala Pro Leu Gly Val Arg Ser Lys Ser Gly Pro Leu Lys Pro
225                 230                 235                 240

Ala Arg Glu Asp Ser Glu Asn Lys Asp His Ala Gly Glu Ile Ser Ser
                245                 250                 255

Leu Pro Phe Pro Gly Val Val Leu Lys Pro Ala Ala Ser Arg Gly Gly
            260                 265                 270

Leu Gly Leu Ser Lys Asn Gly Glu Glu Lys Lys Glu Asp Arg Lys Ile
        275                 280                 285

Asp Ala Ala Lys Asn Thr Phe Gln Ser Lys Ile Asn Gln Glu Glu Leu
    290                 295                 300

Ala Ser Gly Thr Pro Pro Ala Arg Phe Pro Lys Ala Pro Ser Lys Leu
305                 310                 315                 320

Thr Val Gly Gly Pro Trp Gly Gln Ser Gln Glu Lys Glu Lys Gly Asp
                325                 330                 335
```



```
Lys Asn Ser Ala Thr Pro Lys Gln Lys Pro Leu Pro Pro Leu Phe Thr
            340                 345                 350

Leu Gly Pro Pro Pro Pro Lys Pro Asn Arg Pro Pro Asn Val Asp Leu
        355                 360                 365

Thr Lys Phe His Lys Thr Ser Ser Gly Asn Ser Thr Ser Lys Gly Gln
    370                 375                 380

Thr Ser Tyr Ser Thr Thr Ser Leu Pro Pro Pro Pro Pro Ser His Pro
385                 390                 395                 400

Ala Ser Gln Pro Pro Leu Pro Ala Ser His Pro Ser Gln Pro Pro Val
                405                 410                 415

Pro Ser Leu Pro Pro Arg Asn Ile Lys Pro Pro Phe Asp Leu Lys Ser
            420                 425                 430

Pro Val Asn Glu Asp Asn Gln Asp Gly Val Thr His Ser Asp Gly Ala
        435                 440                 445

Gly Asn Leu Asp Glu Glu Gln Asp Ser Glu Gly Glu Thr Tyr Glu Asp
    450                 455                 460

Ile Glu Ala Ser Lys Glu Arg Glu Lys Lys Arg Glu Lys Glu Glu Lys
465                 470                 475                 480

Lys Arg Leu Glu Leu Glu Lys Lys Glu Gln Lys Glu Lys Glu Lys Lys
                485                 490                 495

Glu Gln Glu Ile Lys Lys Lys Phe Lys Leu Thr Gly Pro Ile Gln Val
            500                 505                 510

Ile His Leu Ala Lys Ala Cys Cys Asp Val Lys Gly Gly Lys Asn Glu
        515                 520                 525

Leu Ser Phe Lys Gln Gly Glu Gln Ile Glu Ile Ile Arg Ile Thr Asp
    530                 535                 540

Asn Pro Glu Gly Lys Trp Leu Gly Arg Thr Ala Arg Gly Ser Tyr Gly
545                 550                 555                 560

Tyr Ile Lys Thr Thr Ala Val Glu Ile Asp Tyr Asp Ser Leu Lys Leu
                565                 570                 575

Lys Lys Asp Ser Leu Gly Ala Pro Ser Arg Pro Ile Glu Asp Asp Gln
            580                 585                 590

Glu Val Tyr Asp Asp Val Ala Glu Gln Asp Asp Ile Ser Ser His Ser
        595                 600                 605

Gln Ser Gly Ser Gly Gly Ile Phe Pro Pro Pro Pro Asp Asp Asp Ile
    610                 615                 620

Tyr Asp Gly Ile Glu Glu Glu Asp Ala Asp Asp Gly Phe Pro Ala Pro
625                 630                 635                 640

Pro Lys Gln Leu Asp Met Gly Asp Glu Val Tyr Asp Asp Val Asp Thr
                645                 650                 655
```

Ser Asp Phe Pro Val Ser Ser Ala Glu Met Ser Gln Gly Thr Asn Phe
660 665 670

Gly Lys Ala Lys Thr Glu Glu Lys Asp Leu Lys Lys Leu Lys Lys Gln
675 680 685

Glu Lys Glu Glu Lys Asp Phe Arg Lys Lys Phe Lys Tyr Asp Gly Glu
690 695 700

Ile Arg Val Leu Tyr Ser Thr Lys Val Thr Thr Ser Ile Thr Ser Lys
705 710 715 720

Lys Trp Gly Thr Arg Asp Leu Gln Val Lys Pro Gly Glu Ser Leu Glu
725 730 735

Val Ile Gln Thr Thr Asp Asp Thr Lys Val Leu Cys Arg Asn Glu Glu
740 745 750

Gly Lys Tyr Gly Tyr Val Leu Arg Ser Tyr Leu Ala Asp Asn Asp Gly
755 760 765

Glu Ile Tyr Asp Asp Ile Ala Asp Gly Cys Ile Tyr Asp Asn Asp
770 775 780

<210> 167
<211> 117
<212> PRT
<213> Homo sapiens

<400> 167

Met Ala Ala Ala Ala Ala Ala Gly Ser Gly Thr Pro Arg Glu Glu Glu
1 5 10 15

Val Pro Ala Gly Glu Ala Ala Ala Ser Gln Pro Gln Ala Pro Thr Ser
20 25 30

Val Pro Gly Ala Arg Leu Ser Arg Leu Pro Leu Ala Arg Val Lys Ala
35 40 45

Leu Val Lys Ala Asp Pro Asp Val Thr Leu Ala Gly Gln Glu Ala Ile
50 55 60

Phe Ile Leu Ala Arg Ala Ala Glu Leu Phe Val Glu Thr Ile Ala Lys
65 70 75 80

Asp Ala Tyr Cys Cys Ala Gln Gln Gly Lys Arg Lys Thr Leu Gln Arg
85 90 95

Arg Asp Leu Asp Asn Ala Ile Glu Ala Val Asp Glu Phe Ala Phe Leu
100 105 110

Glu Gly Thr Leu Asp
115

<210> 168
<211> 243
<212> PRT
<213> Homo sapiens

<400> 168

Met Ala Val Gln Ile Ser Lys Arg Arg Lys Phe Val Ala Asp Gly Ile
1 5 10 15

Phe Lys Ala Glu Leu Asn Glu Phe Leu Thr Arg Glu Leu Ala Glu Asp
20 25 30

Gly Tyr Ser Gly Val Glu Val Arg Val Thr Pro Thr Arg Thr Glu Ile
35 40 45

Ile Ile Leu Ala Thr Arg Thr Gln Asn Val Leu Gly Glu Lys Gly Arg
50 55 60

Arg Ile Arg Glu Leu Thr Ala Val Val Gln Lys Arg Phe Gly Phe Pro
65 70 75 80

Glu Gly Ser Val Glu Leu Tyr Ala Glu Lys Val Ala Thr Arg Gly Leu
85 90 95

Cys Ala Ile Ala Gln Ala Glu Ser Leu Arg Tyr Lys Leu Leu Gly Gly
100 105 110

Leu Ala Val Arg Arg Ala Cys Tyr Gly Val Leu Arg Phe Ile Met Glu
115 120 125

Ser Gly Ala Lys Gly Cys Glu Val Val Val Ser Gly Lys Leu Arg Gly
130 135 140

Gln Arg Ala Lys Ser Met Lys Phe Val Asp Gly Leu Met Ile His Ser
145 150 155 160

Gly Asp Pro Val Asn Tyr Tyr Val Asp Thr Ala Val Arg His Val Leu
165 170 175

Leu Arg Gln Gly Val Leu Gly Ile Lys Val Lys Ile Met Leu Pro Trp
180 185 190

Asp Pro Thr Gly Lys Ile Gly Pro Lys Lys Pro Leu Pro Asp His Val
195 200 205

Ser Ile Val Glu Pro Lys Asp Glu Ile Leu Pro Thr Thr Pro Ile Ser
210 215 220

Glu Gln Lys Gly Gly Lys Pro Glu Pro Pro Ala Met Pro Gln Pro Val
225 230 235 240

Pro Thr Ala

<210> 169
<211> 136
<212> PRT
<213> Homo sapiens

<400> 169

Met Val Leu Leu Glu Ser Glu Gln Phe Leu Thr Glu Leu Thr Arg Leu
1 5 10 15

Phe Gln Lys Cys Arg Thr Ser Gly Ser Val Tyr Ile Thr Leu Lys Lys
20 25 30

```
Tyr Asp Gly Arg Thr Lys Pro Ile Pro Lys Lys Gly Thr Val Glu Gly
        35                  40                  45

Phe Glu Pro Ala Asp Asn Lys Cys Leu Leu Arg Ala Thr Asp Gly Lys
    50                  55                  60

Lys Lys Ile Ser Thr Val Val Ser Ser Lys Glu Val Asn Lys Phe Gln
65                  70                  75                  80

Met Ala Tyr Ser Asn Leu Leu Arg Ala Asn Met Asp Gly Leu Lys Lys
                85                  90                  95

Arg Asp Lys Lys Asn Lys Thr Lys Lys Thr Lys Ala Ala Ala Ala Ala
            100                 105                 110

Ala Ala Ala Ala Pro Ala Ala Ala Ala Thr Ala Ala Thr Thr Ala Ala
        115                 120                 125

Thr Thr Ala Ala Thr Ala Ala Gln
    130                 135

<210>  170
<211>  409
<212>  PRT
<213>  Homo sapiens

<400>  170

Met Gln Val Thr Leu Lys Thr Leu Gln Gln Gln Thr Phe Lys Ile Asp
1               5                   10                  15

Ile Asp Pro Glu Glu Thr Val Lys Ala Leu Lys Glu Lys Ile Glu Ser
            20                  25                  30

Glu Lys Gly Lys Asp Ala Phe Pro Val Ala Gly Gln Lys Leu Ile Tyr
        35                  40                  45

Ala Gly Lys Ile Leu Asn Asp Asp Thr Ala Leu Lys Glu Tyr Lys Ile
    50                  55                  60

Asp Glu Lys Asn Phe Val Val Val Met Val Thr Lys Pro Lys Ala Val
65                  70                  75                  80

Ser Thr Pro Ala Pro Ala Thr Thr Gln Gln Ser Ala Pro Ala Ser Thr
                85                  90                  95

Thr Ala Val Thr Ser Ser Thr Thr Thr Thr Val Ala Gln Ala Pro Thr
            100                 105                 110

Pro Val Pro Ala Leu Ala Pro Thr Ser Thr Pro Ala Ser Ile Thr Pro
        115                 120                 125

Ala Ser Ala Thr Ala Ser Ser Glu Pro Ala Pro Ala Ser Ala Ala Lys
    130                 135                 140

Gln Glu Lys Pro Ala Glu Lys Pro Ala Glu Thr Pro Val Ala Thr Ser
145                 150                 155                 160

Pro Thr Ala Thr Asp Ser Thr Ser Gly Asp Ser Ser Arg Ser Asn Leu
                165                 170                 175
```



```
Phe Glu Asp Ala Thr Ser Ala Leu Val Thr Gly Gln Ser Tyr Glu Asn
            180                 185                 190

Met Val Thr Glu Ile Met Ser Met Gly Tyr Glu Arg Glu Gln Val Ile
        195                 200                 205

Ala Ala Leu Arg Ala Ser Phe Asn Asn Pro Asp Arg Ala Val Glu Tyr
    210                 215                 220

Leu Leu Met Gly Ile Pro Gly Asp Arg Glu Ser Gln Ala Val Val Asp
225                 230                 235                 240

Pro Pro Gln Ala Ala Ser Thr Gly Ala Pro Gln Ser Ser Ala Val Ala
                245                 250                 255

Ala Ala Ala Ala Thr Thr Thr Ala Thr Thr Thr Thr Thr Ser Ser Gly
            260                 265                 270

Gly His Pro Leu Glu Phe Leu Arg Asn Gln Pro Gln Phe Gln Gln Met
        275                 280                 285

Arg Gln Ile Ile Gln Gln Asn Pro Ser Leu Leu Pro Ala Leu Leu Gln
    290                 295                 300

Gln Ile Gly Arg Glu Asn Pro Gln Leu Leu Gln Gln Ile Ser Gln His
305                 310                 315                 320

Gln Glu His Phe Ile Gln Met Leu Asn Glu Pro Val Gln Glu Ala Gly
                325                 330                 335

Gly Gln Gly Gly Gly Gly Gly Gly Gly Ser Gly Gly Ile Ala Glu Ala
            340                 345                 350

Gly Ser Gly His Met Asn Tyr Ile Gln Val Thr Pro Gln Glu Lys Glu
        355                 360                 365

Ala Ile Glu Arg Leu Lys Ala Leu Gly Phe Pro Glu Gly Leu Val Ile
    370                 375                 380

Gln Ala Tyr Phe Ala Cys Glu Lys Asn Glu Asn Leu Ala Ala Asn Phe
385                 390                 395                 400

Leu Leu Gln Gln Asn Phe Asp Glu Asp
                405

<210>  171
<211>  614
<212>  PRT
<213>  Homo sapiens

<400>  171

Met Ser Gly Ile Lys Lys Gln Lys Thr Glu Asn Gln Gln Lys Ser Thr
1               5                   10                  15

Asn Val Val Tyr Gln Ala His His Val Ser Arg Asn Lys Arg Gly Gln
            20                  25                  30

Val Val Gly Thr Arg Gly Gly Phe Arg Gly Cys Thr Val Trp Leu Thr
        35                  40                  45
```

```
Gly Leu Ser Gly Ala Gly Lys Thr Thr Ile Ser Phe Ala Leu Glu Glu
     50                  55                  60

Tyr Leu Val Ser His Ala Ile Pro Cys Tyr Ser Leu Asp Gly Asp Asn
65                  70                  75                  80

Val Arg His Gly Leu Asn Arg Asn Leu Gly Phe Ser Pro Gly Asp Arg
                85                  90                  95

Glu Glu Asn Ile Arg Arg Ile Ala Glu Val Ala Lys Leu Phe Ala Asp
            100                 105                 110

Ala Gly Leu Val Cys Ile Thr Ser Phe Ile Ser Pro Phe Ala Lys Asp
        115                 120                 125

Arg Glu Asn Ala Arg Lys Ile His Glu Ser Ala Gly Leu Pro Phe Phe
    130                 135                 140

Glu Ile Phe Val Asp Ala Pro Leu Asn Ile Cys Glu Ser Arg Asp Val
145                 150                 155                 160

Lys Gly Leu Tyr Lys Lys Ala Arg Ala Gly Glu Ile Lys Gly Phe Thr
                165                 170                 175

Gly Ile Asp Ser Asp Tyr Glu Lys Pro Glu Thr Pro Glu Arg Val Leu
            180                 185                 190

Lys Thr Asn Leu Ser Thr Val Ser Asp Cys Val His Gln Val Val Glu
        195                 200                 205

Leu Leu Gln Glu Gln Asn Ile Val Pro Tyr Thr Ile Ile Lys Asp Ile
    210                 215                 220

His Glu Leu Phe Val Pro Glu Asn Lys Leu Asp His Val Arg Ala Glu
225                 230                 235                 240

Ala Glu Thr Leu Pro Ser Leu Ser Ile Thr Lys Leu Asp Leu Gln Trp
                245                 250                 255

Val Gln Val Leu Ser Glu Gly Trp Ala Thr Pro Leu Lys Gly Phe Met
            260                 265                 270

Arg Glu Lys Glu Tyr Leu Gln Val Met His Phe Asp Thr Leu Leu Asp
        275                 280                 285

Asp Gly Val Ile Asn Met Ser Ile Pro Ile Val Leu Pro Val Ser Ala
    290                 295                 300

Glu Asp Lys Thr Arg Leu Glu Gly Cys Ser Lys Phe Val Leu Ala His
305                 310                 315                 320

Gly Gly Arg Arg Val Ala Ile Leu Arg Asp Ala Glu Phe Tyr Glu His
                325                 330                 335

Arg Lys Glu Glu Arg Cys Ser Arg Val Trp Gly Thr Thr Cys Thr Lys
            340                 345                 350

His Pro His Ile Lys Met Val Met Glu Ser Gly Asp Trp Leu Val Gly
        355                 360                 365
```



```
Gly Asp Leu Gln Val Leu Glu Lys Ile Arg Trp Asn Asp Gly Leu Asp
    370                 375                 380

Gln Tyr Arg Leu Thr Pro Leu Glu Leu Lys Gln Lys Cys Lys Glu Met
385                 390                 395                 400

Asn Ala Asp Ala Val Phe Ala Phe Gln Leu Arg Asn Pro Val His Asn
                405                 410                 415

Gly His Ala Leu Leu Met Gln Asp Thr Arg Arg Arg Leu Leu Glu Arg
            420                 425                 430

Gly Tyr Lys His Pro Val Leu Leu Leu His Pro Leu Gly Gly Trp Thr
        435                 440                 445

Lys Asp Asp Asp Val Pro Leu Asp Trp Arg Met Lys Gln His Ala Ala
    450                 455                 460

Val Leu Glu Glu Gly Val Leu Asp Pro Lys Ser Thr Ile Val Ala Ile
465                 470                 475                 480

Phe Pro Ser Pro Met Leu Tyr Ala Gly Pro Thr Glu Val Gln Trp His
                485                 490                 495

Cys Arg Ser Arg Met Ile Ala Gly Ala Asn Phe Tyr Ile Val Gly Arg
            500                 505                 510

Asp Pro Ala Gly Met Pro His Pro Glu Thr Lys Lys Asp Leu Tyr Glu
        515                 520                 525

Pro Thr His Gly Gly Lys Val Leu Ser Met Ala Pro Gly Leu Thr Ser
    530                 535                 540

Val Glu Ile Ile Pro Phe Arg Val Ala Ala Tyr Asn Lys Ala Lys Lys
545                 550                 555                 560

Ala Met Asp Phe Tyr Asp Leu Ala Arg His Asn Glu Phe Asp Phe Ile
                565                 570                 575

Ser Gly Thr Arg Met Arg Lys Leu Ala Arg Glu Gly Glu Asn Pro Pro
            580                 585                 590

Asp Gly Phe Met Ala Pro Lys Ala Trp Lys Val Leu Thr Asp Tyr Tyr
        595                 600                 605

Arg Ser Leu Glu Lys Asn
    610
```

<210> 172
<211> 798
<212> PRT
<213> Homo sapiens

<400> 172

```
Met Asn Leu Gln Pro Ile Phe Trp Ile Gly Leu Ile Ser Ser Val Cys
1               5                   10                  15

Cys Val Phe Ala Gln Thr Asp Glu Asn Arg Cys Leu Lys Ala Asn Ala
            20                  25                  30
```

```
Lys Ser Cys Gly Glu Cys Ile Gln Ala Gly Pro Asn Cys Gly Trp Cys
        35                  40                  45

Thr Asn Ser Thr Phe Leu Gln Glu Gly Met Pro Thr Ser Ala Arg Cys
    50                  55                  60

Asp Asp Leu Glu Ala Leu Lys Lys Lys Gly Cys Pro Pro Asp Asp Ile
65                  70                  75                  80

Glu Asn Pro Arg Gly Ser Lys Asp Ile Lys Lys Asn Lys Asn Val Thr
                85                  90                  95

Asn Arg Ser Lys Gly Thr Ala Glu Lys Leu Lys Pro Glu Asp Ile His
            100                 105                 110

Gln Ile Gln Pro Gln Gln Leu Val Leu Arg Leu Arg Ser Gly Glu Pro
        115                 120                 125

Gln Thr Phe Thr Leu Lys Phe Lys Arg Ala Glu Asp Tyr Pro Ile Asp
    130                 135                 140

Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp Asp Leu Glu
145                 150                 155                 160

Asn Val Lys Ser Leu Gly Thr Asp Leu Met Asn Glu Met Arg Arg Ile
                165                 170                 175

Thr Ser Asp Phe Arg Ile Gly Phe Gly Ser Phe Val Glu Lys Thr Val
            180                 185                 190

Met Pro Tyr Ile Ser Thr Thr Pro Ala Lys Leu Arg Asn Pro Cys Thr
        195                 200                 205

Ser Glu Gln Asn Cys Thr Thr Pro Phe Ser Tyr Lys Asn Val Leu Ser
    210                 215                 220

Leu Thr Asn Lys Gly Glu Val Phe Asn Glu Leu Val Gly Lys Gln Arg
225                 230                 235                 240

Ile Ser Gly Asn Leu Asp Ser Pro Glu Gly Gly Phe Asp Ala Ile Met
                245                 250                 255

Gln Val Ala Val Cys Gly Ser Leu Ile Gly Trp Arg Asn Val Thr Arg
            260                 265                 270

Leu Leu Val Phe Ser Thr Asp Ala Gly Phe His Phe Ala Gly Asp Gly
        275                 280                 285

Lys Leu Gly Gly Ile Val Leu Pro Asn Asp Gly Gln Cys His Leu Glu
    290                 295                 300

Asn Asn Met Tyr Thr Met Ser His Tyr Tyr Asp Tyr Pro Ser Ile Ala
305                 310                 315                 320

His Leu Val Gln Lys Leu Ser Glu Asn Asn Ile Gln Thr Ile Phe Ala
                325                 330                 335

Val Thr Glu Glu Phe Gln Pro Val Tyr Lys Glu Leu Lys Asn Leu Ile
```



```
            340                 345                 350

Pro Lys Ser Ala Val Gly Thr Leu Ser Ala Asn Ser Ser Asn Val Ile
        355                 360                 365

Gln Leu Ile Ile Asp Ala Tyr Asn Ser Leu Ser Ser Glu Val Ile Leu
    370                 375                 380

Glu Asn Gly Lys Leu Ser Glu Gly Val Thr Ile Ser Tyr Lys Ser Tyr
385                 390                 395                 400

Cys Lys Asn Gly Val Asn Gly Thr Gly Glu Asn Gly Arg Lys Cys Ser
                405                 410                 415

Asn Ile Ser Ile Gly Asp Glu Val Gln Phe Glu Ile Ser Ile Thr Ser
            420                 425                 430

Asn Lys Cys Pro Lys Lys Asp Ser Asp Ser Phe Lys Ile Arg Pro Leu
        435                 440                 445

Gly Phe Thr Glu Glu Val Glu Val Ile Leu Gln Tyr Ile Cys Glu Cys
    450                 455                 460

Glu Cys Gln Ser Glu Gly Ile Pro Glu Ser Pro Lys Cys His Glu Gly
465                 470                 475                 480

Asn Gly Thr Phe Glu Cys Gly Ala Cys Arg Cys Asn Glu Gly Arg Val
                485                 490                 495

Gly Arg His Cys Glu Cys Ser Thr Asp Glu Val Asn Ser Glu Asp Met
            500                 505                 510

Asp Ala Tyr Cys Arg Lys Glu Asn Ser Ser Glu Ile Cys Ser Asn Asn
        515                 520                 525

Gly Glu Cys Val Cys Gly Gln Cys Val Cys Arg Lys Arg Asp Asn Thr
    530                 535                 540

Asn Glu Ile Tyr Ser Gly Lys Phe Cys Glu Cys Asp Asn Phe Asn Cys
545                 550                 555                 560

Asp Arg Ser Asn Gly Leu Ile Cys Gly Gly Asn Gly Val Cys Lys Cys
                565                 570                 575

Arg Val Cys Glu Cys Asn Pro Asn Tyr Thr Gly Ser Ala Cys Asp Cys
            580                 585                 590

Ser Leu Asp Thr Ser Thr Cys Glu Ala Ser Asn Gly Gln Ile Cys Asn
        595                 600                 605

Gly Arg Gly Ile Cys Glu Cys Gly Val Cys Lys Cys Thr Asp Pro Lys
    610                 615                 620

Phe Gln Gly Gln Thr Cys Glu Met Cys Gln Thr Cys Leu Gly Val Cys
625                 630                 635                 640

Ala Glu His Lys Glu Cys Val Gln Cys Arg Ala Phe Asn Lys Gly Glu
                645                 650                 655
```

```
Lys Lys Asp Thr Cys Thr Gln Glu Cys Ser Tyr Phe Asn Ile Thr Lys
            660                 665                 670

Val Glu Ser Arg Asp Lys Leu Pro Gln Pro Val Gln Pro Asp Pro Val
        675                 680                 685

Ser His Cys Lys Glu Lys Asp Val Asp Asp Cys Trp Phe Tyr Phe Thr
    690                 695                 700

Tyr Ser Val Asn Gly Asn Asn Glu Val Met Val His Val Val Glu Asn
705                 710                 715                 720

Pro Glu Cys Pro Thr Gly Pro Asp Ile Ile Pro Ile Val Ala Gly Val
                725                 730                 735

Val Ala Gly Ile Val Leu Ile Gly Leu Ala Leu Leu Leu Ile Trp Lys
            740                 745                 750

Leu Leu Met Ile Ile His Asp Arg Arg Glu Phe Ala Lys Phe Glu Lys
        755                 760                 765

Glu Lys Met Asn Ala Lys Trp Asp Thr Gly Glu Asn Pro Ile Tyr Lys
    770                 775                 780

Ser Ala Val Thr Thr Val Val Asn Pro Lys Tyr Glu Gly Lys
785                 790                 795
```

<210> 173
<211> 502
<212> PRT
<213> Homo sapiens

<400> 173

```
Met Ala Ser Lys Lys Leu Gly Ala Asp Phe His Gly Thr Phe Ser Tyr
1               5                   10                  15

Leu Asp Asp Val Pro Phe Lys Thr Gly Asp Lys Phe Lys Thr Pro Ala
            20                  25                  30

Lys Val Gly Leu Pro Ile Gly Phe Ser Leu Pro Asp Cys Leu Gln Val
        35                  40                  45

Val Arg Glu Val Gln Tyr Asp Phe Ser Leu Glu Lys Lys Thr Ile Glu
    50                  55                  60

Trp Ala Glu Glu Ile Lys Lys Ile Glu Glu Ala Glu Arg Glu Ala Glu
65                  70                  75                  80

Cys Lys Ile Ala Glu Ala Glu Ala Lys Val Asn Ser Lys Ser Gly Pro
                85                  90                  95

Glu Gly Asp Ser Lys Met Ser Phe Ser Lys Thr His Ser Thr Ala Thr
            100                 105                 110

Met Pro Pro Pro Ile Asn Pro Ile Leu Ala Ser Leu Gln His Asn Ser
        115                 120                 125

Ile Leu Thr Pro Thr Arg Val Ser Ser Ser Ala Thr Lys Gln Lys Val
    130                 135                 140
```



```
Leu Ser Pro Pro His Ile Lys Ala Asp Phe Asn Leu Ala Asp Phe Glu
145                 150                 155                 160

Cys Glu Glu Asp Pro Phe Asp Asn Leu Glu Leu Lys Thr Ile Asp Glu
                165                 170                 175

Lys Glu Glu Leu Arg Asn Ile Leu Val Gly Thr Thr Gly Pro Ile Met
            180                 185                 190

Ala Gln Leu Leu Asp Asn Asn Leu Pro Arg Gly Gly Ser Gly Ser Val
        195                 200                 205

Leu Gln Asp Glu Glu Val Leu Ala Ser Leu Glu Arg Ala Thr Leu Asp
    210                 215                 220

Phe Lys Pro Leu His Lys Pro Asn Gly Phe Ile Thr Leu Pro Gln Leu
225                 230                 235                 240

Gly Asn Cys Glu Lys Met Ser Leu Ser Ser Lys Val Ser Leu Pro Pro
                245                 250                 255

Ile Pro Ala Val Ser Asn Ile Lys Ser Leu Ser Phe Pro Lys Leu Asp
            260                 265                 270

Ser Asp Asp Ser Asn Gln Lys Thr Ala Lys Leu Ala Ser Thr Phe His
        275                 280                 285

Ser Thr Ser Cys Leu Arg Asn Gly Thr Phe Gln Asn Ser Leu Lys Pro
    290                 295                 300

Ser Thr Gln Ser Ser Ala Ser Glu Leu Asn Gly His His Thr Leu Gly
305                 310                 315                 320

Leu Ser Ala Leu Asn Leu Asp Ser Gly Thr Glu Met Pro Ala Leu Thr
                325                 330                 335

Ser Ser Gln Met Pro Ser Leu Ser Val Leu Ser Val Cys Thr Glu Glu
            340                 345                 350

Ser Ser Pro Pro Asn Thr Gly Pro Thr Val Thr Pro Pro Asn Phe Ser
        355                 360                 365

Val Ser Gln Val Pro Asn Met Pro Ser Cys Pro Gln Ala Tyr Ser Glu
    370                 375                 380

Leu Gln Met Leu Ser Pro Ser Glu Arg Gln Cys Val Glu Thr Val Val
385                 390                 395                 400

Asn Met Gly Tyr Ser Tyr Glu Cys Val Leu Arg Ala Met Lys Lys Lys
                405                 410                 415

Gly Glu Asn Ile Glu Gln Ile Leu Asp Tyr Leu Phe Ala His Gly Gln
            420                 425                 430

Leu Cys Glu Lys Gly Phe Asp Pro Leu Leu Val Glu Glu Ala Leu Glu
        435                 440                 445

Met His Gln Cys Ser Glu Glu Lys Met Met Glu Phe Leu Gln Leu Met
    450                 455                 460
```

```
Ser Lys Phe Lys Glu Met Gly Phe Glu Leu Lys Asp Ile Lys Glu Val
465                 470                 475                 480

Leu Leu Leu His Asn Asn Asp Gln Asp Asn Ala Leu Glu Asp Leu Met
                485                 490                 495

Ala Arg Ala Gly Ala Ser
            500
```

<210> 174
<211> 545
<212> PRT
<213> Homo sapiens

<400> 174

```
Met Ser Asn Asn Gly Leu Asp Ile Gln Asp Lys Pro Pro Ala Pro Pro
1               5                   10                  15

Met Arg Asn Thr Ser Thr Met Ile Gly Val Gly Ser Lys Asp Ala Gly
            20                  25                  30

Thr Leu Asn His Gly Ser Lys Pro Leu Pro Pro Asn Pro Glu Glu Lys
        35                  40                  45

Lys Lys Lys Asp Arg Phe Tyr Arg Ser Ile Leu Pro Gly Asp Lys Thr
    50                  55                  60

Asn Lys Lys Lys Glu Lys Glu Arg Pro Glu Ile Ser Leu Pro Ser Asp
65                  70                  75                  80

Phe Glu His Thr Ile His Val Gly Phe Asp Ala Val Thr Gly Glu Phe
                85                  90                  95

Thr Gly Met Pro Glu Gln Trp Ala Arg Leu Leu Gln Thr Ser Asn Ile
            100                 105                 110

Thr Lys Ser Glu Gln Lys Lys Asn Pro Gln Ala Val Leu Asp Val Leu
        115                 120                 125

Glu Phe Tyr Asn Ser Lys Lys Thr Ser Asn Ser Gln Lys Tyr Met Ser
    130                 135                 140

Phe Thr Asp Lys Ser Ala Glu Asp Tyr Asn Ser Ser Asn Ala Leu Asn
145                 150                 155                 160

Val Lys Ala Val Ser Glu Thr Pro Ala Val Pro Pro Val Ser Glu Asp
                165                 170                 175

Glu Asp Asp Asp Asp Asp Asp Ala Thr Pro Pro Pro Val Ile Ala Pro
            180                 185                 190

Arg Pro Glu His Thr Lys Ser Val Tyr Thr Arg Ser Val Ile Glu Pro
        195                 200                 205

Leu Pro Val Thr Pro Thr Arg Asp Val Ala Thr Ser Pro Ile Ser Pro
    210                 215                 220

Thr Glu Asn Asn Thr Thr Pro Pro Asp Ala Leu Thr Arg Asn Thr Glu
225                 230                 235                 240
```



```
Lys Gln Lys Lys Lys Pro Lys Met Ser Asp Glu Glu Ile Leu Glu Lys
                245                 250                 255

Leu Arg Ser Ile Val Ser Val Gly Asp Pro Lys Lys Lys Tyr Thr Arg
            260                 265                 270

Phe Glu Lys Ile Gly Gln Gly Ala Ser Gly Thr Val Tyr Thr Ala Met
        275                 280                 285

Asp Val Ala Thr Gly Gln Glu Val Ala Ile Lys Gln Met Asn Leu Gln
    290                 295                 300

Gln Gln Pro Lys Lys Glu Leu Ile Ile Asn Glu Ile Leu Val Met Arg
305                 310                 315                 320

Glu Asn Lys Asn Pro Asn Ile Val Asn Tyr Leu Asp Ser Tyr Leu Val
                325                 330                 335

Gly Asp Glu Leu Trp Val Val Met Glu Tyr Leu Ala Gly Gly Ser Leu
            340                 345                 350

Thr Asp Val Val Thr Glu Thr Cys Met Asp Glu Gly Gln Ile Ala Ala
        355                 360                 365

Val Cys Arg Glu Cys Leu Gln Ala Leu Glu Phe Leu His Ser Asn Gln
    370                 375                 380

Val Ile His Arg Asp Ile Lys Ser Asp Asn Ile Leu Leu Gly Met Asp
385                 390                 395                 400

Gly Ser Val Lys Leu Thr Asp Phe Gly Phe Cys Ala Gln Ile Thr Pro
                405                 410                 415

Glu Gln Ser Lys Arg Ser Thr Met Val Gly Thr Pro Tyr Trp Met Ala
            420                 425                 430

Pro Glu Val Val Thr Arg Lys Ala Tyr Gly Pro Lys Val Asp Ile Trp
        435                 440                 445

Ser Leu Gly Ile Met Ala Ile Glu Met Ile Glu Gly Glu Pro Pro Tyr
    450                 455                 460

Leu Asn Glu Asn Pro Leu Arg Ala Leu Tyr Leu Ile Ala Thr Asn Gly
465                 470                 475                 480

Thr Pro Glu Leu Gln Asn Pro Glu Lys Leu Ser Ala Ile Phe Arg Asp
                485                 490                 495

Phe Leu Asn Arg Cys Leu Asp Met Asp Val Glu Lys Arg Gly Ser Ala
            500                 505                 510

Lys Glu Leu Leu Gln His Gln Phe Leu Lys Ile Ala Lys Pro Leu Ser
        515                 520                 525

Ser Leu Thr Pro Leu Ile Ala Ala Ala Lys Glu Ala Thr Lys Asn Asn
    530                 535                 540

His
545
```

<210> 175
<211> 1360
<212> PRT
<213> Homo sapiens

<400> 175

Met Ser Arg Gln Ser Thr Leu Tyr Ser Phe Phe Pro Lys Ser Pro Ala
1 5 10 15

Leu Ser Asp Ala Asn Lys Ala Ser Ala Arg Ala Ser Arg Glu Gly Gly
20 25 30

Arg Ala Ala Ala Ala Pro Gly Ala Ser Pro Ser Pro Gly Gly Asp Ala
35 40 45

Ala Trp Ser Glu Ala Gly Pro Gly Pro Arg Pro Leu Ala Arg Ser Ala
50 55 60

Ser Pro Pro Lys Ala Lys Asn Leu Asn Gly Gly Leu Arg Arg Ser Val
65 70 75 80

Ala Pro Ala Ala Pro Thr Ser Cys Asp Phe Ser Pro Gly Asp Leu Val
85 90 95

Trp Ala Lys Met Glu Gly Tyr Pro Trp Trp Pro Cys Leu Val Tyr Asn
100 105 110

His Pro Phe Asp Gly Thr Phe Ile Arg Glu Lys Gly Lys Ser Val Arg
115 120 125

Val His Val Gln Phe Phe Asp Asp Ser Pro Thr Arg Gly Trp Val Ser
130 135 140

Lys Arg Leu Leu Lys Pro Tyr Thr Gly Ser Lys Ser Lys Glu Ala Gln
145 150 155 160

Lys Gly Gly His Phe Tyr Ser Ala Lys Pro Glu Ile Leu Arg Ala Met
165 170 175

Gln Arg Ala Asp Glu Ala Leu Asn Lys Asp Lys Ile Lys Arg Leu Glu
180 185 190

Leu Ala Val Cys Asp Glu Pro Ser Glu Pro Glu Glu Glu Glu Glu Met
195 200 205

Glu Val Gly Thr Thr Tyr Val Thr Asp Lys Ser Glu Glu Asp Asn Glu
210 215 220

Ile Glu Ser Glu Glu Glu Val Gln Pro Lys Thr Gln Gly Ser Arg Arg
225 230 235 240

Ser Ser Arg Gln Ile Lys Lys Arg Arg Val Ile Ser Asp Ser Glu Ser
245 250 255

Asp Ile Gly Gly Ser Asp Val Glu Phe Lys Pro Asp Thr Lys Glu Glu
260 265 270

Gly Ser Ser Asp Glu Ile Ser Ser Gly Val Gly Asp Ser Glu Ser Glu
275 280 285

Gly Leu Asn Ser Pro Val Lys Val Ala Arg Lys Arg Lys Arg Met Val
290 295 300

Thr Gly Asn Gly Ser Leu Lys Arg Lys Ser Ser Arg Lys Glu Thr Pro
305 310 315 320

Ser Ala Thr Lys Gln Ala Thr Ser Ile Ser Ser Glu Thr Lys Asn Thr
325 330 335

Leu Arg Ala Phe Ser Ala Pro Gln Asn Ser Glu Ser Gln Ala His Val
340 345 350

Ser Gly Gly Gly Asp Asp Ser Ser Arg Pro Thr Val Trp Tyr His Glu
355 360 365

Thr Leu Glu Trp Leu Lys Glu Glu Lys Arg Arg Asp Glu His Arg Arg
370 375 380

Arg Pro Asp His Pro Asp Phe Asp Ala Ser Thr Leu Tyr Val Pro Glu
385 390 395 400

Asp Phe Leu Asn Ser Cys Thr Pro Gly Met Arg Lys Trp Trp Gln Ile
405 410 415

Lys Ser Gln Asn Phe Asp Leu Val Ile Cys Tyr Lys Val Gly Lys Phe
420 425 430

Tyr Glu Leu Tyr His Met Asp Ala Leu Ile Gly Val Ser Glu Leu Gly
435 440 445

Leu Val Phe Met Lys Gly Asn Trp Ala His Ser Gly Phe Pro Glu Ile
450 455 460

Ala Phe Gly Arg Tyr Ser Asp Ser Leu Val Gln Lys Gly Tyr Lys Val
465 470 475 480

Ala Arg Val Glu Gln Thr Glu Thr Pro Glu Met Met Glu Ala Arg Cys
485 490 495

Arg Lys Met Ala His Ile Ser Lys Tyr Asp Arg Val Val Arg Arg Glu
500 505 510

Ile Cys Arg Ile Ile Thr Lys Gly Thr Gln Thr Tyr Ser Val Leu Glu
515 520 525

Gly Asp Pro Ser Glu Asn Tyr Ser Lys Tyr Leu Leu Ser Leu Lys Glu
530 535 540

Lys Glu Glu Asp Ser Ser Gly His Thr Arg Ala Tyr Gly Val Cys Phe
545 550 555 560

Val Asp Thr Ser Leu Gly Lys Phe Phe Ile Gly Gln Phe Ser Asp Asp
565 570 575

Arg His Cys Ser Arg Phe Arg Thr Leu Val Ala His Tyr Pro Pro Val
580 585 590

Gln Val Leu Phe Glu Lys Gly Asn Leu Ser Lys Glu Thr Lys Thr Ile

595 600 605

Leu Lys Ser Ser Leu Ser Cys Ser Leu Gln Glu Gly Leu Ile Pro Gly
610 615 620

Ser Gln Phe Trp Asp Ala Ser Lys Thr Leu Arg Thr Leu Leu Glu Glu
625 630 635 640

Glu Tyr Phe Arg Glu Lys Leu Ser Asp Gly Ile Gly Val Met Leu Pro
645 650 655

Gln Val Leu Lys Gly Met Thr Ser Glu Ser Asp Ser Ile Gly Leu Thr
660 665 670

Pro Gly Glu Lys Ser Glu Leu Ala Leu Ser Ala Leu Gly Gly Cys Val
675 680 685

Phe Tyr Leu Lys Lys Cys Leu Ile Asp Gln Glu Leu Leu Ser Met Ala
690 695 700

Asn Phe Glu Glu Tyr Ile Pro Leu Asp Ser Asp Thr Val Ser Thr Thr
705 710 715 720

Arg Ser Gly Ala Ile Phe Thr Lys Ala Tyr Gln Arg Met Val Leu Asp
725 730 735

Ala Val Thr Leu Asn Asn Leu Glu Ile Phe Leu Asn Gly Thr Asn Gly
740 745 750

Ser Thr Glu Gly Thr Leu Leu Glu Arg Val Asp Thr Cys His Thr Pro
755 760 765

Phe Gly Lys Arg Leu Leu Lys Gln Trp Leu Cys Ala Pro Leu Cys Asn
770 775 780

His Tyr Ala Ile Asn Asp Arg Leu Asp Ala Ile Glu Asp Leu Met Val
785 790 795 800

Val Pro Asp Lys Ile Ser Glu Val Val Glu Leu Leu Lys Lys Leu Pro
805 810 815

Asp Leu Glu Arg Leu Leu Ser Lys Ile His Asn Val Gly Ser Pro Leu
820 825 830

Lys Ser Gln Asn His Pro Asp Ser Arg Ala Ile Met Tyr Glu Glu Thr
835 840 845

Thr Tyr Ser Lys Lys Lys Ile Ile Asp Phe Leu Ser Ala Leu Glu Gly
850 855 860

Phe Lys Val Met Cys Lys Ile Ile Gly Ile Met Glu Glu Val Ala Asp
865 870 875 880

Gly Phe Lys Ser Lys Ile Leu Lys Gln Val Ile Ser Leu Gln Thr Lys
885 890 895

Asn Pro Glu Gly Arg Phe Pro Asp Leu Thr Val Glu Leu Asn Arg Trp
900 905 910

Asp Thr Ala Phe Asp His Glu Lys Ala Arg Lys Thr Gly Leu Ile Thr
915 920 925

Pro Lys Ala Gly Phe Asp Ser Asp Tyr Asp Gln Ala Leu Ala Asp Ile
930 935 940

Arg Glu Asn Glu Gln Ser Leu Leu Glu Tyr Leu Glu Lys Gln Arg Asn
945 950 955 960

Arg Ile Gly Cys Arg Thr Ile Val Tyr Trp Gly Ile Gly Arg Asn Arg
965 970 975

Tyr Gln Leu Glu Ile Pro Glu Asn Phe Thr Thr Arg Asn Leu Pro Glu
980 985 990

Glu Tyr Glu Leu Lys Ser Thr Lys Lys Gly Cys Lys Arg Tyr Trp Thr
995 1000 1005

Lys Thr Ile Glu Lys Lys Leu Ala Asn Leu Ile Asn Ala Glu Glu
1010 1015 1020

Arg Arg Asp Val Ser Leu Lys Asp Cys Met Arg Arg Leu Phe Tyr
1025 1030 1035

Asn Phe Asp Lys Asn Tyr Lys Asp Trp Gln Ser Ala Val Glu Cys
1040 1045 1050

Ile Ala Val Leu Asp Val Leu Leu Cys Leu Ala Asn Tyr Ser Arg
1055 1060 1065

Gly Gly Asp Gly Pro Met Cys Arg Pro Val Ile Leu Leu Pro Glu
1070 1075 1080

Asp Thr Pro Pro Phe Leu Glu Leu Lys Gly Ser Arg His Pro Cys
1085 1090 1095

Ile Thr Lys Thr Phe Phe Gly Asp Asp Phe Ile Pro Asn Asp Ile
1100 1105 1110

Leu Ile Gly Cys Glu Glu Glu Glu Gln Glu Asn Gly Lys Ala Tyr
1115 1120 1125

Cys Val Leu Val Thr Gly Pro Asn Met Gly Gly Lys Ser Thr Leu
1130 1135 1140

Met Arg Gln Ala Gly Leu Leu Ala Val Met Ala Gln Met Gly Cys
1145 1150 1155

Tyr Val Pro Ala Glu Val Cys Arg Leu Thr Pro Ile Asp Arg Val
1160 1165 1170

Phe Thr Arg Leu Gly Ala Ser Asp Arg Ile Met Ser Gly Glu Ser
1175 1180 1185

Thr Phe Phe Val Glu Leu Ser Glu Thr Ala Ser Ile Leu Met His
1190 1195 1200

Ala Thr Ala His Ser Leu Val Leu Val Asp Glu Leu Gly Arg Gly
1205 1210 1215

```
Thr Ala  Thr Phe Asp Gly Thr  Ala Ile Ala Asn Ala  Val Val Lys
    1220                1225                1230

Glu Leu  Ala Glu Thr Ile Lys  Cys Arg Thr Leu Phe  Ser Thr His
    1235                1240                1245

Tyr His  Ser Leu Val Glu Asp  Tyr Ser Gln Asn Val  Ala Val Arg
    1250                1255                1260

Leu Gly  His Met Ala Cys Met  Val Glu Asn Glu Cys  Glu Asp Pro
    1265                1270                1275

Ser Gln  Glu Thr Ile Thr Phe  Leu Tyr Lys Phe Ile  Lys Gly Ala
    1280                1285                1290

Cys Pro  Lys Ser Tyr Gly Phe  Asn Ala Ala Arg Leu  Ala Asn Leu
    1295                1300                1305

Pro Glu  Glu Val Ile Gln Lys  Gly His Arg Lys Ala  Arg Glu Phe
    1310                1315                1320

Glu Lys  Met Asn Gln Ser Leu  Arg Leu Phe Arg Glu  Val Cys Leu
    1325                1330                1335

Ala Ser  Glu Arg Ser Thr Val  Asp Ala Glu Ala Val  His Lys Leu
    1340                1345                1350

Leu Thr  Leu Ile Lys Glu Leu
    1355                1360


<210>  176
<211>  398
<212>  PRT
<213>  Homo sapiens

<400>  176

Met Gln Ser Glu Arg Gly Ile Thr Ile Asp Ile Ser Leu Trp Lys Phe
1               5                  10                  15

Glu Thr Ser Lys Tyr Tyr Val Thr Ile Ile Asp Ala Pro Gly His Arg
            20                  25                  30

Asp Phe Ile Gln Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala
        35                  40                  45

Val Leu Ile Val Ala Ala Gly Val Gly Glu Phe Glu Ala Gly Ile Ser
    50                  55                  60

Lys Asn Gly Gln Thr Arg Glu His Ala Leu Leu Ala Tyr Thr Leu Gly
65                  70                  75                  80

Val Lys Gln Leu Ile Val Gly Val Asn Lys Met Asp Ser Thr Glu Pro
                85                  90                  95

Pro Tyr Ser Gln Lys Arg Tyr Glu Glu Ile Val Lys Glu Val Ser Thr
            100                 105                 110

Tyr Ile Lys Lys Ile Gly Tyr Asn Pro Asp Thr Val Ala Phe Val Pro
        115                 120                 125
```



```
Ile Ser Gly Trp Asn Gly Asp Asn Met Leu Glu Pro Ser Ala Asn Met
    130                 135                 140

Pro Trp Phe Lys Gly Trp Lys Val Thr Arg Lys Asp Gly Asn Ala Ser
145                 150                 155                 160

Gly Thr Thr Leu Leu Glu Ala Leu Asp Cys Ile Leu Pro Pro Thr Arg
                165                 170                 175

Pro Thr Asp Lys Pro Leu Gly Leu Pro Leu Gln Asp Val Tyr Lys Ile
            180                 185                 190

Gly Gly Ile Gly Thr Val Pro Val Gly Arg Val Glu Thr Gly Val Leu
        195                 200                 205

Lys Pro Gly Met Val Val Thr Phe Gly Pro Val Asn Val Thr Thr Glu
    210                 215                 220

Val Lys Ser Val Glu Met His His Glu Ala Leu Gly Glu Ala Leu Pro
225                 230                 235                 240

Gly Asp Asn Val Gly Phe Asn Val Lys Asn Val Ser Val Lys Asp Val
                245                 250                 255

Arg Arg Gly Asn Val Ala Gly Asp Ser Lys Asn Asp Pro Pro Met Glu
            260                 265                 270

Ala Ala Gly Phe Pro Ala Gln Val Ile Ile Leu Asn His Pro Gly Gln
        275                 280                 285

Ile Ser Ala Gly Tyr Ala Pro Val Leu Asp Cys His Thr Ala His Ile
    290                 295                 300

Ala Cys Lys Phe Ala Glu Leu Lys Glu Lys Ile Asp Arg Arg Ser Gly
305                 310                 315                 320

Lys Lys Leu Glu Asp Gly Pro Lys Phe Leu Lys Ser Gly Asp Ala Ala
                325                 330                 335

Ile Val Asp Met Val Pro Gly Lys Pro Met Cys Val Glu Ser Phe Ser
            340                 345                 350

Asp Tyr Pro Pro Leu Gly Cys Phe Ala Val Arg Asp Met Arg Gln Thr
        355                 360                 365

Val Ala Val Gly Val Ile Lys Ala Val Asp Lys Lys Ala Ala Gly Ala
    370                 375                 380

Gly Lys Val Thr Lys Ser Ala Gln Lys Ala Gln Lys Ala Lys
385                 390                 395


<210>  177
<211>  334
<212>  PRT
<213>  Homo sapiens

<400>  177

Met Ala Thr Leu Lys Glu Lys Leu Ile Ala Pro Val Ala Glu Glu Glu
1               5                  10                  15
```

```
Ala Thr Val Pro Asn Asn Lys Ile Thr Val Val Gly Val Gly Gln Val
            20                  25                  30

Gly Met Ala Cys Ala Ile Ser Ile Leu Gly Lys Ser Leu Ala Asp Glu
        35                  40                  45

Leu Ala Leu Val Asp Val Leu Glu Asp Lys Leu Lys Gly Glu Met Met
    50                  55                  60

Asp Leu Gln His Gly Ser Leu Phe Leu Gln Thr Pro Lys Ile Val Ala
65                  70                  75                  80

Asp Lys Asp Tyr Ser Val Thr Ala Asn Ser Lys Ile Val Val Val Thr
                85                  90                  95

Ala Gly Val Arg Gln Gln Glu Gly Glu Ser Arg Leu Asn Leu Val Gln
            100                 105                 110

Arg Asn Val Asn Val Phe Lys Phe Ile Ile Pro Gln Ile Val Lys Tyr
        115                 120                 125

Ser Pro Asp Cys Ile Ile Ile Val Val Ser Asn Pro Val Asp Ile Leu
    130                 135                 140

Thr Tyr Val Thr Trp Lys Leu Ser Gly Leu Pro Lys His Arg Val Ile
145                 150                 155                 160

Gly Ser Gly Cys Asn Leu Asp Ser Ala Arg Phe Arg Tyr Leu Met Ala
                165                 170                 175

Glu Lys Leu Gly Ile His Pro Ser Ser Cys His Gly Trp Ile Leu Gly
            180                 185                 190

Glu His Gly Asp Ser Ser Val Ala Val Trp Ser Gly Val Asn Val Ala
        195                 200                 205

Gly Val Ser Leu Gln Glu Leu Asn Pro Glu Met Gly Thr Asp Asn Asp
    210                 215                 220

Ser Glu Asn Trp Lys Glu Val His Lys Met Val Val Glu Ser Ala Tyr
225                 230                 235                 240

Glu Val Ile Lys Leu Lys Gly Tyr Thr Asn Trp Ala Ile Gly Leu Ser
                245                 250                 255

Val Ala Asp Leu Ile Glu Ser Met Leu Lys Asn Leu Ser Arg Ile His
            260                 265                 270

Pro Val Ser Thr Met Val Lys Gly Met Tyr Gly Ile Glu Asn Glu Val
        275                 280                 285

Phe Leu Ser Leu Pro Cys Ile Leu Asn Ala Arg Gly Leu Thr Ser Val
    290                 295                 300

Ile Asn Gln Lys Leu Lys Asp Asp Glu Val Ala Gln Leu Lys Lys Ser
305                 310                 315                 320

Ala Asp Thr Leu Trp Asp Ile Gln Lys Asp Leu Lys Asp Leu
                325                 330
```


<210> 178
<211> 364
<212> PRT
<213> Homo sapiens

<400> 178

```
Met Tyr Leu Ser Arg Phe Leu Ser Ile His Ala Leu Trp Val Thr Val
1               5                   10                  15

Ser Ser Val Met Gln Pro Tyr Pro Leu Val Trp Gly His Tyr Asp Leu
            20                  25                  30

Cys Lys Thr Gln Ile Tyr Thr Glu Glu Gly Lys Val Trp Asp Tyr Met
        35                  40                  45

Ala Cys Gln Pro Glu Ser Thr Asp Met Thr Lys Tyr Leu Lys Val Lys
    50                  55                  60

Leu Asp Pro Pro Asp Ile Thr Cys Gly Asp Pro Pro Glu Thr Phe Cys
65                  70                  75                  80

Ala Met Gly Asn Pro Tyr Met Cys Asn Asn Glu Cys Asp Ala Ser Thr
                85                  90                  95

Pro Glu Leu Ala His Pro Pro Glu Leu Met Phe Asp Phe Glu Gly Arg
            100                 105                 110

His Pro Ser Thr Phe Trp Gln Ser Ala Thr Trp Lys Glu Tyr Pro Lys
        115                 120                 125

Pro Leu Gln Val Asn Ile Thr Leu Ser Trp Ser Lys Thr Ile Glu Leu
    130                 135                 140

Thr Asp Asn Ile Val Ile Thr Phe Glu Ser Gly Arg Pro Asp Gln Met
145                 150                 155                 160

Ile Leu Glu Lys Ser Leu Asp Tyr Gly Arg Thr Trp Gln Pro Tyr Gln
                165                 170                 175

Tyr Tyr Ala Thr Asp Cys Leu Asp Ala Phe His Met Asp Pro Lys Ser
            180                 185                 190

Val Lys Asp Leu Ser Gln His Thr Val Leu Glu Ile Ile Cys Thr Glu
        195                 200                 205

Glu Tyr Ser Thr Gly Tyr Thr Thr Asn Ser Lys Ile Ile His Phe Glu
    210                 215                 220

Ile Lys Asp Arg Phe Ala Phe Phe Ala Gly Pro Arg Leu Arg Asn Met
225                 230                 235                 240

Ala Ser Leu Tyr Gly Gln Leu Asp Thr Thr Lys Lys Leu Arg Asp Phe
                245                 250                 255

Phe Thr Val Thr Asp Leu Arg Ile Arg Leu Leu Arg Pro Ala Val Gly
            260                 265                 270

Glu Ile Phe Val Asp Glu Leu His Leu Ala Arg Tyr Phe Tyr Ala Ile
        275                 280                 285
```

```
Ser Asp Ile Lys Val Arg Gly Arg Cys Lys Cys Asn Leu His Ala Thr
    290                 295                 300

Val Cys Val Tyr Asp Asn Ser Lys Leu Thr Cys Glu Cys Glu His Asn
305                 310                 315                 320

Thr Thr Gly Pro Asp Cys Gly Lys Cys Lys Lys Asn Tyr Gln Gly Arg
                325                 330                 335

Pro Trp Ser Pro Gly Ser Tyr Leu Pro Ile Pro Lys Gly Thr Ala Asn
            340                 345                 350

Thr Cys Ile Pro Ser Ile Ser Ser Ile Gly Ser Lys
        355                 360
```

<210> 179
<211> 416
<212> PRT
<213> Homo sapiens

<400> 179

```
Met His Thr Asp Pro Asp Tyr Ser Ala Ala Tyr Val Val Ile Glu Thr
1               5                   10                  15

Asp Ala Glu Asp Gly Ile Lys Gly Cys Gly Ile Thr Phe Thr Leu Gly
            20                  25                  30

Lys Gly Thr Glu Val Val Val Cys Ala Val Asn Ala Leu Ala His His
        35                  40                  45

Val Leu Asn Lys Asp Leu Lys Asp Ile Val Gly Asp Phe Arg Gly Phe
    50                  55                  60

Tyr Arg Gln Leu Thr Ser Asp Gly Gln Leu Arg Trp Ile Gly Pro Glu
65                  70                  75                  80

Lys Gly Val Val His Leu Ala Thr Ala Ala Val Leu Asn Ala Val Trp
                85                  90                  95

Asp Leu Trp Ala Lys Gln Glu Gly Lys Pro Val Trp Lys Leu Leu Val
            100                 105                 110

Asp Met Asp Pro Arg Met Leu Val Ser Cys Ile Asp Phe Arg Tyr Ile
        115                 120                 125

Thr Asp Val Leu Thr Glu Glu Asp Ala Leu Glu Ile Leu Gln Lys Gly
    130                 135                 140

Gln Ile Gly Lys Lys Glu Arg Glu Lys Gln Met Leu Ala Gln Gly Tyr
145                 150                 155                 160

Pro Ala Tyr Thr Thr Ser Cys Ala Trp Leu Gly Tyr Ser Asp Asp Thr
                165                 170                 175

Leu Lys Gln Leu Cys Ala Gln Ala Leu Lys Asp Gly Trp Thr Arg Phe
            180                 185                 190

Lys Val Lys Val Gly Ala Asp Leu Gln Asp Asp Met Arg Arg Cys Gln
        195                 200                 205
```



```
Ile Ile Arg Asp Met Ile Gly Pro Glu Lys Thr Leu Met Met Asp Ala
    210                 215                 220

Asn Gln Arg Trp Asp Val Pro Glu Ala Val Glu Trp Met Ser Lys Leu
225                 230                 235                 240

Ala Lys Phe Lys Pro Leu Trp Ile Glu Glu Pro Thr Ser Pro Asp Asp
                245                 250                 255

Ile Leu Gly His Ala Thr Ile Ser Lys Ala Leu Val Pro Leu Gly Ile
            260                 265                 270

Gly Ile Ala Thr Gly Glu Gln Cys His Asn Arg Val Ile Phe Lys Gln
        275                 280                 285

Leu Leu Gln Ala Lys Ala Leu Gln Phe Leu Gln Ile Asp Ser Cys Arg
    290                 295                 300

Leu Gly Ser Val Asn Glu Asn Leu Ser Val Leu Leu Met Ala Lys Lys
305                 310                 315                 320

Phe Glu Ile Pro Val Cys Pro His Ala Gly Gly Val Gly Leu Cys Glu
                325                 330                 335

Leu Val Gln His Leu Ile Ile Phe Asp Tyr Ile Ser Val Ser Ala Ser
            340                 345                 350

Leu Glu Asn Arg Val Cys Glu Tyr Val Asp His Leu His Glu His Phe
        355                 360                 365

Lys Tyr Pro Val Met Ile Gln Arg Ala Ser Tyr Met Pro Pro Lys Asp
    370                 375                 380

Pro Gly Tyr Ser Thr Glu Met Lys Glu Glu Ser Val Lys Lys His Gln
385                 390                 395                 400

Tyr Pro Asp Gly Glu Val Trp Lys Lys Leu Leu Pro Ala Gln Glu Asn
                405                 410                 415
```

<210> 180
<211> 89
<212> PRT
<213> Homo sapiens

<400> 180

```
Met Ser Ser Gln Gln Gln Lys Gln Pro Cys Ile Pro Pro Pro Gln Leu
1               5                   10                  15

Gln Gln Gln Gln Val Lys Gln Pro Cys Gln Pro Pro Pro Gln Glu Pro
            20                  25                  30

Cys Ile Pro Lys Thr Lys Glu Pro Cys His Pro Lys Val Pro Glu Pro
        35                  40                  45

Cys His Pro Lys Val Pro Glu Pro Cys Gln Pro Lys Leu Pro Glu Pro
    50                  55                  60

Cys His Pro Lys Val Pro Glu Pro Cys Pro Ser Ile Val Thr Pro Ala
65                  70                  75                  80
```

Pro Ala Gln Gln Lys Thr Lys Gln Lys
85

<210> 181
<211> 253
<212> PRT
<213> Homo sapiens

<400> 181

Met Ala Arg Ser Leu Leu Leu Pro Leu Gln Ile Leu Leu Leu Ser Leu
1 5 10 15

Ala Leu Glu Thr Ala Gly Glu Glu Ala Gln Gly Asp Lys Ile Ile Asp
20 25 30

Gly Ala Pro Cys Ala Arg Gly Ser His Pro Trp Gln Val Ala Leu Leu
35 40 45

Ser Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn Glu Arg Trp
50 55 60

Val Leu Thr Ala Ala His Cys Lys Met Asn Glu Tyr Thr Val His Leu
65 70 75 80

Gly Ser Asp Thr Leu Gly Asp Arg Arg Ala Gln Arg Ile Lys Ala Ser
85 90 95

Lys Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His Val Asn Asp
100 105 110

Leu Met Leu Val Lys Leu Asn Ser Gln Ala Arg Leu Ser Ser Met Val
115 120 125

Lys Lys Val Arg Leu Pro Ser Arg Cys Glu Pro Pro Gly Thr Thr Cys
130 135 140

Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro
145 150 155 160

Ser Asp Leu Met Cys Val Asp Val Lys Leu Ile Ser Pro Gln Asp Cys
165 170 175

Thr Lys Val Tyr Lys Asp Leu Leu Glu Asn Ser Met Leu Cys Ala Gly
180 185 190

Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro
195 200 205

Leu Val Cys Arg Gly Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Phe
210 215 220

Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys
225 230 235 240

Phe Thr Lys Trp Ile Asn Asp Thr Met Lys Lys His Arg
245 250

<210> 182
<211> 169

<212> PRT
<213> Homo sapiens

<400> 182

Met Leu Ala Thr Arg Val Phe Ser Leu Val Gly Lys Arg Ala Ile Ser
1 5 10 15

Thr Ser Val Cys Val Arg Ala His Glu Ser Val Val Lys Ser Glu Asp
20 25 30

Phe Ser Leu Pro Ala Tyr Met Asp Arg Arg Asp His Pro Leu Pro Glu
35 40 45

Val Ala His Val Lys His Leu Ser Ala Ser Gln Lys Ala Leu Lys Glu
50 55 60

Lys Glu Lys Ala Ser Trp Ser Ser Leu Ser Met Asp Glu Lys Val Glu
65 70 75 80

Leu Tyr Arg Ile Lys Phe Lys Glu Ser Phe Ala Glu Met Asn Arg Gly
85 90 95

Ser Asn Glu Trp Lys Thr Val Val Gly Gly Ala Met Phe Phe Ile Gly
100 105 110

Phe Thr Ala Leu Val Ile Met Trp Gln Lys His Tyr Val Tyr Gly Pro
115 120 125

Leu Pro Gln Ser Phe Asp Lys Glu Trp Val Ala Lys Gln Thr Lys Arg
130 135 140

Met Leu Asp Met Lys Val Asn Pro Ile Gln Gly Leu Ala Ser Lys Trp
145 150 155 160

Asp Tyr Glu Lys Asn Glu Trp Lys Lys
165

<210> 183
<211> 879
<212> PRT
<213> Homo sapiens

<400> 183

Met Ala Gly Gly Gly Gly Asp Leu Ser Thr Arg Arg Leu Asn Glu Cys
1 5 10 15

Ile Ser Pro Val Ala Asn Glu Met Asn His Leu Pro Ala His Ser His
20 25 30

Asp Leu Gln Arg Met Phe Thr Glu Asp Gln Gly Val Asp Asp Arg Leu
35 40 45

Leu Tyr Asp Ile Val Phe Lys His Phe Lys Arg Asn Lys Val Glu Ile
50 55 60

Ser Asn Ala Ile Lys Lys Thr Phe Pro Phe Leu Glu Gly Leu Arg Asp
65 70 75 80

Arg Asp Leu Ile Thr Asn Lys Met Phe Glu Asp Ser Gln Asp Ser Cys
85 90 95

```
Arg Asn Leu Val Pro Val Gln Arg Val Val Tyr Asn Val Leu Ser Glu
            100                 105                 110

Leu Glu Lys Thr Phe Asn Leu Pro Val Leu Glu Ala Leu Phe Ser Asp
        115                 120                 125

Val Asn Met Gln Glu Tyr Pro Asp Leu Ile His Ile Tyr Lys Gly Phe
    130                 135                 140

Glu Asn Val Ile His Asp Lys Leu Pro Leu Gln Glu Ser Glu Glu Glu
145                 150                 155                 160

Glu Arg Glu Glu Arg Ser Gly Leu Gln Leu Ser Leu Glu Gln Gly Thr
                165                 170                 175

Gly Glu Asn Ser Phe Arg Ser Leu Thr Trp Pro Pro Ser Gly Ser Pro
            180                 185                 190

Ser His Ala Gly Thr Thr Pro Pro Glu Asn Gly Leu Ser Glu His Pro
        195                 200                 205

Cys Glu Thr Glu Gln Ile Asn Ala Lys Arg Lys Asp Thr Thr Ser Asp
    210                 215                 220

Lys Asp Asp Ser Leu Gly Ser Gln Gln Thr Asn Glu Gln Cys Ala Gln
225                 230                 235                 240

Lys Ala Glu Pro Thr Glu Ser Cys Glu Gln Ile Ala Val Gln Val Asn
                245                 250                 255

Asn Gly Asp Ala Gly Arg Glu Met Pro Cys Pro Leu Pro Cys Asp Glu
            260                 265                 270

Glu Ser Pro Glu Ala Glu Leu His Asn His Gly Ile Gln Ile Asn Ser
        275                 280                 285

Cys Ser Val Arg Leu Val Asp Ile Lys Lys Glu Lys Pro Phe Ser Asn
    290                 295                 300

Ser Lys Val Glu Cys Gln Ala Gln Ala Arg Thr His His Asn Gln Ala
305                 310                 315                 320

Ser Asp Ile Ile Val Ile Ser Ser Glu Asp Ser Glu Gly Ser Thr Asp
                325                 330                 335

Val Asp Glu Pro Leu Glu Val Phe Ile Ser Ala Pro Arg Ser Glu Pro
            340                 345                 350

Val Ile Asn Asn Asp Asn Pro Leu Glu Ser Asn Asp Glu Lys Glu Gly
        355                 360                 365

Gln Glu Ala Thr Cys Ser Arg Pro Gln Ile Val Pro Glu Pro Met Asp
    370                 375                 380

Phe Arg Lys Leu Ser Thr Phe Arg Glu Ser Phe Lys Lys Arg Val Ile
385                 390                 395                 400

Gly Gln Asp His Asp Phe Ser Glu Ser Ser Glu Glu Glu Ala Pro Ala
                405                 410                 415
```



```
Glu Ala Ser Ser Gly Ala Leu Arg Ser Lys His Gly Glu Lys Ala Pro
            420                 425                 430

Met Thr Ser Arg Ser Thr Ser Thr Trp Arg Ile Pro Ser Arg Lys Arg
        435                 440                 445

Arg Phe Ser Ser Ser Asp Phe Ser Asp Leu Ser Asn Gly Glu Glu Leu
    450                 455                 460

Gln Glu Thr Cys Ser Ser Ser Leu Arg Arg Gly Ser Gly Ser Gln Pro
465                 470                 475                 480

Gln Glu Pro Glu Asn Lys Lys Cys Ser Cys Val Met Cys Phe Pro Lys
                485                 490                 495

Gly Val Pro Arg Ser Gln Glu Ala Arg Thr Glu Ser Ser Gln Ala Ser
            500                 505                 510

Asp Met Met Asp Thr Met Asp Val Glu Asn Asn Ser Thr Leu Glu Lys
        515                 520                 525

His Ser Gly Lys Arg Arg Lys Lys Arg Arg His Arg Ser Lys Val Asn
    530                 535                 540

Gly Leu Gln Arg Gly Arg Lys Lys Asp Arg Pro Arg Lys His Leu Thr
545                 550                 555                 560

Leu Asn Asn Lys Val Gln Lys Lys Arg Trp Gln Gln Arg Gly Arg Lys
                565                 570                 575

Ala Asn Thr Arg Pro Leu Lys Arg Arg Arg Lys Arg Gly Pro Arg Ile
            580                 585                 590

Pro Lys Asp Glu Asn Ile Asn Phe Lys Gln Ser Glu Leu Pro Val Thr
        595                 600                 605

Cys Gly Glu Val Lys Gly Thr Leu Tyr Lys Glu Arg Phe Lys Gln Gly
    610                 615                 620

Thr Ser Lys Lys Cys Ile Gln Ser Glu Asp Lys Lys Trp Phe Thr Pro
625                 630                 635                 640

Arg Glu Phe Glu Ile Glu Gly Asp Arg Gly Ala Ser Lys Asn Trp Lys
                645                 650                 655

Leu Ser Ile Arg Cys Gly Gly Tyr Thr Leu Lys Val Leu Met Glu Asn
            660                 665                 670

Lys Phe Leu Pro Glu Pro Pro Ser Thr Arg Lys Lys Arg Ile Leu Glu
        675                 680                 685

Ser His Asn Asn Thr Leu Val Asp Pro Cys Glu Glu His Lys Lys Lys
    690                 695                 700

Asn Pro Asp Ala Ser Val Lys Phe Ser Glu Phe Leu Lys Lys Cys Ser
705                 710                 715                 720

Glu Thr Trp Lys Thr Ile Phe Ala Lys Glu Lys Gly Lys Phe Glu Asp
```

725 730 735

Met Ala Lys Ala Asp Lys Ala His Tyr Glu Arg Glu Met Lys Thr Tyr
740 745 750

Ile Pro Pro Lys Gly Glu Lys Lys Lys Lys Phe Lys Asp Pro Asn Ala
755 760 765

Pro Lys Arg Pro Pro Leu Ala Phe Phe Leu Phe Cys Ser Glu Tyr Arg
770 775 780

Pro Lys Ile Lys Gly Glu His Pro Gly Leu Ser Ile Asp Asp Val Val
785 790 795 800

Lys Lys Leu Ala Gly Met Trp Asn Asn Thr Ala Ala Ala Asp Lys Gln
805 810 815

Phe Tyr Glu Lys Lys Ala Ala Lys Leu Lys Glu Lys Tyr Lys Lys Asp
820 825 830

Ile Ala Ala Tyr Arg Ala Lys Gly Lys Pro Asn Ser Ala Lys Lys Arg
835 840 845

Val Val Lys Ala Glu Lys Ser Lys Lys Lys Lys Glu Glu Glu Glu Asp
850 855 860

Glu Glu Asp Glu Gln Glu Glu Glu Asn Glu Glu Asp Asp Asp Lys
865 870 875

<210> 184
<211> 316
<212> PRT
<213> Homo sapiens

<400> 184

Met Ala Ser Thr Ser Arg Leu Asp Ala Leu Pro Arg Val Thr Cys Pro
1 5 10 15

Asn His Pro Asp Ala Ile Leu Val Glu Asp Tyr Arg Ala Gly Asp Met
20 25 30

Ile Cys Pro Glu Cys Gly Leu Val Val Gly Asp Arg Val Ile Asp Val
35 40 45

Gly Ser Glu Trp Arg Thr Phe Ser Asn Asp Lys Ala Thr Lys Asp Pro
50 55 60

Ser Arg Val Gly Asp Ser Gln Asn Pro Leu Leu Ser Asp Gly Asp Leu
65 70 75 80

Ser Thr Met Ile Gly Lys Gly Thr Gly Ala Ala Ser Phe Asp Glu Phe
85 90 95

Gly Asn Ser Lys Tyr Gln Asn Arg Arg Thr Met Ser Ser Ser Asp Arg
100 105 110

Ala Met Met Asn Ala Phe Lys Glu Ile Thr Thr Met Ala Asp Arg Ile
115 120 125

Asn Leu Pro Arg Asn Ile Val Asp Arg Thr Asn Asn Leu Phe Lys Gln

130 135 140

Val Tyr Glu Gln Lys Ser Leu Lys Gly Arg Ala Asn Asp Ala Ile Ala
145 150 155 160

Ser Ala Cys Leu Tyr Ile Ala Cys Arg Gln Glu Gly Val Pro Arg Thr
165 170 175

Phe Lys Glu Ile Cys Ala Val Ser Arg Ile Ser Lys Lys Glu Ile Gly
180 185 190

Arg Cys Phe Lys Leu Ile Leu Lys Ala Leu Glu Thr Ser Val Asp Leu
195 200 205

Ile Thr Thr Gly Asp Phe Met Ser Arg Phe Cys Ser Asn Leu Cys Leu
210 215 220

Pro Lys Gln Val Gln Met Ala Ala Thr His Ile Ala Arg Lys Ala Val
225 230 235 240

Glu Leu Asp Leu Val Pro Gly Arg Ser Pro Ile Ser Val Ala Ala Ala
245 250 255

Ala Ile Tyr Met Ala Ser Gln Ala Ser Ala Glu Lys Arg Thr Gln Lys
260 265 270

Glu Ile Gly Asp Ile Ala Gly Val Ala Asp Val Thr Ile Arg Gln Ser
275 280 285

Tyr Arg Leu Ile Tyr Pro Arg Ala Pro Asp Leu Phe Pro Thr Asp Phe
290 295 300

Lys Phe Asp Thr Pro Val Asp Lys Leu Pro Gln Leu
305 310 315

<210> 185
<211> 628
<212> PRT
<213> Homo sapiens

<400> 185

Ala Asp Phe Leu Asp Ala Leu Ile Val Ser Met Asp Val Ile Gln His
1 5 10 15

Glu Thr Ile Gly Lys Lys Phe Glu Lys Arg His Ile Glu Ile Phe Thr
20 25 30

Asp Leu Ser Ser Arg Phe Ser Lys Ser Gln Leu Asp Ile Ile Ile His
35 40 45

Ser Leu Lys Lys Cys Asp Ile Ser Leu Gln Phe Phe Leu Pro Phe Ser
50 55 60

Leu Gly Lys Glu Asp Gly Ser Gly Asp Arg Gly Asp Gly Pro Phe Arg
65 70 75 80

Leu Gly Gly His Gly Pro Ser Phe Pro Leu Lys Gly Ile Thr Glu Gln
85 90 95

Gln Lys Glu Gly Leu Glu Ile Val Lys Met Val Met Ile Ser Leu Glu

```
            100                 105                 110

Gly Glu Asp Gly Leu Asp Glu Ile Tyr Ser Phe Ser Glu Ser Leu Arg
        115                 120                 125

Lys Leu Cys Val Phe Lys Lys Ile Glu Arg His Ser Ile His Trp Pro
    130                 135                 140

Cys Arg Leu Thr Ile Gly Ser Asn Leu Ser Ile Arg Ile Ala Ala Tyr
145                 150                 155                 160

Lys Ser Ile Leu Gln Glu Arg Val Lys Lys Thr Trp Thr Val Val Asp
                165                 170                 175

Ala Lys Thr Leu Lys Lys Glu Asp Ile Gln Lys Glu Thr Val Tyr Cys
            180                 185                 190

Leu Asn Asp Asp Asp Glu Thr Glu Val Leu Lys Glu Asp Ile Ile Gln
        195                 200                 205

Gly Phe Leu Tyr Gly Ser Asp Ile Val Pro Phe Ser Lys Val Asp Glu
    210                 215                 220

Glu Gln Met Lys Tyr Lys Ser Glu Gly Lys Cys Phe Ser Val Leu Gly
225                 230                 235                 240

Phe Cys Lys Ser Ser Gln Val Gln Arg Arg Phe Phe Met Gly Asn Gln
                245                 250                 255

Val Leu Lys Val Phe Ala Ala Arg Asp Asp Glu Ala Ala Ala Val Ala
            260                 265                 270

Leu Ser Ser Leu Ile His Ala Leu Asp Asp Leu Asp Met Val Ala Ile
        275                 280                 285

Val Arg Tyr Ala Tyr Asp Lys Arg Ala Asn Pro Gln Val Gly Val Ala
    290                 295                 300

Phe Pro His Ile Lys His Asn Tyr Glu Cys Leu Val Tyr Val Gln Leu
305                 310                 315                 320

Pro Phe Met Glu Asp Leu Arg Gln Tyr Met Phe Ser Ser Leu Lys Asn
                325                 330                 335

Ser Lys Lys Tyr Ala Pro Thr Glu Ala Gln Leu Asn Ala Val Asp Ala
            340                 345                 350

Leu Ile Asp Ser Met Ser Leu Ala Lys Lys Asp Glu Lys Thr Asp Thr
        355                 360                 365

Leu Glu Asp Leu Phe Pro Thr Thr Lys Ile Pro Asn Pro Arg Phe Gln
    370                 375                 380

Arg Leu Phe Gln Cys Leu Leu His Arg Ala Leu His Pro Arg Glu Pro
385                 390                 395                 400

Leu Pro Pro Ile Gln Gln His Ile Trp Asn Met Leu Asn Pro Pro Ala
                405                 410                 415
```



```
Glu Val Thr Thr Lys Ser Gln Ile Pro Leu Ser Lys Ile Lys Thr Leu
            420                 425                 430

Phe Pro Leu Ile Glu Ala Lys Lys Lys Asp Gln Val Thr Ala Gln Glu
        435                 440                 445

Ile Phe Gln Asp Asn His Glu Asp Gly Pro Thr Ala Lys Lys Leu Lys
    450                 455                 460

Thr Glu Gln Gly Gly Ala His Phe Ser Val Ser Ser Leu Ala Glu Gly
465                 470                 475                 480

Ser Val Thr Ser Val Gly Ser Val Asn Pro Ala Glu Asn Phe Arg Val
                485                 490                 495

Leu Val Lys Gln Lys Lys Ala Ser Phe Glu Glu Ala Ser Asn Gln Leu
            500                 505                 510

Ile Asn His Ile Glu Gln Phe Leu Asp Thr Asn Glu Thr Pro Tyr Phe
        515                 520                 525

Met Lys Ser Ile Asp Cys Ile Arg Ala Phe Arg Glu Glu Ala Ile Lys
    530                 535                 540

Phe Ser Glu Glu Gln Arg Phe Asn Asn Phe Leu Lys Ala Leu Gln Glu
545                 550                 555                 560

Lys Val Glu Ile Lys Gln Leu Asn His Phe Trp Glu Ile Val Val Gln
                565                 570                 575

Asp Gly Ile Thr Leu Ile Thr Lys Glu Glu Ala Ser Gly Ser Ser Val
            580                 585                 590

Thr Ala Glu Glu Ala Lys Lys Phe Leu Ala Pro Lys Asp Lys Pro Ser
        595                 600                 605

Gly Asp Thr Ala Ala Val Phe Glu Glu Gly Gly Asp Val Asp Asp Leu
    610                 615                 620

Leu Asp Met Ile
625
```

<210> 186
<211> 420
<212> PRT
<213> Homo sapiens

<400> 186

```
Met Gly Ser Gly Trp Lys Lys Ile Lys Leu Gln Met Lys Cys Asp Gly
1               5                   10                  15

Cys Ser Glu Gln Gly Ser His Pro Cys Ala Phe Ile Gly Ile Gly Asn
            20                  25                  30

Ser Asp Gln Glu Met Gln Gln Leu Asn Leu Glu Gly Lys Asn Tyr Cys
        35                  40                  45

Thr Ala Lys Thr Leu Tyr Ile Ser Asp Ser Asp Lys Gln Lys His Phe
    50                  55                  60
```

```
Met Leu Ser Val Lys Val Phe Tyr Gly Asn Gly Asp Asp Ile Gly Val
65                  70                  75                  80

Phe Leu Ser Lys Ser Ser Lys Pro Ser Lys Lys Lys Gln Ser Leu Lys
                85                  90                  95

Asn Ala Asp Leu Cys Ile Gly Ser Gly Thr Lys Val Ala Leu Phe Asn
            100                 105                 110

Arg Leu Arg Ser Gln Thr Val Ser Thr Arg Tyr Leu His Val Glu Gly
        115                 120                 125

Gly Asn Phe His Ala Ser Ser Gln Gln Trp Gly Ala Phe Thr Leu Phe
    130                 135                 140

Leu Asp Asp Asp Gly Ser Glu Gly Glu Glu Phe Thr Val Arg Asp Gly
145                 150                 155                 160

Tyr Ile His Tyr Gly Gln Thr Val Lys Leu Val Cys Ser Val Thr Gly
                165                 170                 175

Met Ala Leu Pro Arg Leu Ile Ile Arg Lys Val Asp Lys Gln Thr Thr
            180                 185                 190

Leu Leu Asp Ala Asp Asp Pro Val Ser Gln Leu His Lys Cys Ala Phe
        195                 200                 205

Asp Leu Glu Asp Thr Glu Arg Met Tyr Leu Cys Leu Ser Gln Glu Arg
    210                 215                 220

Ile Ile Gln Phe Gln Ala Thr Pro Cys Pro Thr Glu Pro Asn Lys Glu
225                 230                 235                 240

Met Ile Asn Asp Gly Ala Ser Trp Ala Ile Ile Ser Thr His Lys Ala
                245                 250                 255

Lys Tyr Thr Phe Tyr Glu Arg Met Gly Pro Val Leu Ala Leu Val Met
            260                 265                 270

Pro Met Pro Val Val Glu Ser Leu Lys Leu Asn Gly Gly Gly Asp Glu
        275                 280                 285

Ala Met Leu Glu Leu Thr Gly Gln Asn Phe Thr Pro Asn Leu Arg Val
    290                 295                 300

Trp Phe Gly Asp Val Glu Ala Glu Thr Met Tyr Arg Cys Gly Glu Ser
305                 310                 315                 320

Met Leu Arg Val Val Pro Asp Val Leu His Ser Glu Lys Val Gly Asp
                325                 330                 335

Ser Ser Gln Gln Pro Val Gln Val Ser Val Thr Leu Val Arg Asn Asp
            340                 345                 350

Gly Ile Ile Tyr Ser Thr Ser Leu Thr Phe Thr Tyr Thr Pro Glu Ala
        355                 360                 365

Gly Pro Arg Pro His Cys Ser Val Ala Gly Ala Ile Leu Lys Ala Ser
    370                 375                 380
```



```
Ser Ser His Val Pro Pro Asn Glu Leu Asn Thr Asn Ser Asp Gly Ser
385                 390                 395                 400

Tyr Thr Asn Ala Ser Thr Asn Ser Thr Ser Val Thr Ser Ser Thr Pro
                405                 410                 415

Thr Val Val Ser
            420
```

<210> 187
<211> 103
<212> PRT
<213> Homo sapiens

<400> 187

```
Met Glu Thr Val Gln Glu Leu Ile Pro Leu Ala Lys Glu Met Met Ala
1               5                   10                  15

Gln Lys Arg Lys Gly Lys Met Val Lys Leu Tyr Val Leu Gly Ser Val
            20                  25                  30

Leu Ala Leu Phe Gly Val Val Leu Gly Leu Met Glu Thr Val Cys Ser
        35                  40                  45

Pro Phe Thr Ala Ala Arg Arg Leu Arg Asp Gln Glu Ala Ala Val Ala
    50                  55                  60

Glu Leu Gln Ala Ala Leu Glu Arg Gln Ala Leu Gln Lys Gln Ala Leu
65                  70                  75                  80

Gln Glu Lys Gly Lys Gln Gln Asp Thr Val Leu Gly Gly Arg Ala Leu
                85                  90                  95

Ser Asn Arg Gln His Ala Ser
            100
```

<210> 188
<211> 1306
<212> PRT
<213> Homo sapiens

<400> 188

```
Met Gly Ala Ala Ser Gly Arg Arg Gly Pro Gly Leu Leu Leu Pro Leu
1               5                   10                  15

Pro Leu Leu Leu Leu Leu Pro Pro Gln Pro Ala Leu Ala Leu Asp Pro
            20                  25                  30

Gly Leu Gln Pro Gly Asn Phe Ser Ala Asp Glu Ala Gly Ala Gln Leu
        35                  40                  45

Phe Ala Gln Ser Tyr Asn Ser Ser Ala Glu Gln Val Leu Phe Gln Ser
    50                  55                  60

Val Ala Ala Ser Trp Ala His Asp Thr Asn Ile Thr Ala Glu Asn Ala
65                  70                  75                  80

Arg Arg Gln Glu Glu Ala Ala Leu Leu Ser Gln Glu Phe Ala Glu Ala
                85                  90                  95
```

```
Trp Gly Gln Lys Ala Lys Glu Leu Tyr Glu Pro Ile Trp Gln Asn Phe
            100                 105                 110

Thr Asp Pro Gln Leu Arg Arg Ile Ile Gly Ala Val Arg Thr Leu Gly
        115                 120                 125

Ser Ala Asn Leu Pro Leu Ala Lys Arg Gln Gln Tyr Asn Ala Leu Leu
    130                 135                 140

Ser Asn Met Ser Arg Ile Tyr Ser Thr Ala Lys Val Cys Leu Pro Asn
145                 150                 155                 160

Lys Thr Ala Thr Cys Trp Ser Leu Asp Pro Asp Leu Thr Asn Ile Leu
                165                 170                 175

Ala Ser Ser Arg Ser Tyr Ala Met Leu Leu Phe Ala Trp Glu Gly Trp
            180                 185                 190

His Asn Ala Ala Gly Ile Pro Leu Lys Pro Leu Tyr Glu Asp Phe Thr
        195                 200                 205

Ala Leu Ser Asn Glu Ala Tyr Lys Gln Asp Gly Phe Thr Asp Thr Gly
    210                 215                 220

Ala Tyr Trp Arg Ser Trp Tyr Asn Ser Pro Thr Phe Glu Asp Asp Leu
225                 230                 235                 240

Glu His Leu Tyr Gln Gln Leu Glu Pro Leu Tyr Leu Asn Leu His Ala
                245                 250                 255

Phe Val Arg Arg Ala Leu His Arg Arg Tyr Gly Asp Arg Tyr Ile Asn
            260                 265                 270

Leu Arg Gly Pro Ile Pro Ala His Leu Leu Gly Asp Met Trp Ala Gln
        275                 280                 285

Ser Trp Glu Asn Ile Tyr Asp Met Val Val Pro Phe Pro Asp Lys Pro
    290                 295                 300

Asn Leu Asp Val Thr Ser Thr Met Leu Gln Gln Gly Trp Asn Ala Thr
305                 310                 315                 320

His Met Phe Arg Val Ala Glu Glu Phe Phe Thr Ser Leu Glu Leu Ser
                325                 330                 335

Pro Met Pro Pro Glu Phe Trp Glu Gly Ser Met Leu Glu Lys Pro Ala
            340                 345                 350

Asp Gly Arg Glu Val Val Cys His Ala Ser Ala Trp Asp Phe Tyr Asn
        355                 360                 365

Arg Lys Asp Phe Arg Ile Lys Gln Cys Thr Arg Val Thr Met Asp Gln
    370                 375                 380

Leu Ser Thr Val His His Glu Met Gly His Ile Gln Tyr Tyr Leu Gln
385                 390                 395                 400

Tyr Lys Asp Leu Pro Val Ser Leu Arg Arg Gly Ala Asn Pro Gly Phe
                405                 410                 415
```



```
His Glu Ala Ile Gly Asp Val Leu Ala Leu Ser Val Ser Thr Pro Glu
            420                 425                 430

His Leu His Lys Ile Gly Leu Leu Asp Arg Val Thr Asn Asp Thr Glu
        435                 440                 445

Ser Asp Ile Asn Tyr Leu Leu Lys Met Ala Leu Glu Lys Ile Ala Phe
    450                 455                 460

Leu Pro Phe Gly Tyr Leu Val Asp Gln Trp Arg Trp Gly Val Phe Ser
465                 470                 475                 480

Gly Arg Thr Pro Pro Ser Arg Tyr Asn Phe Asp Trp Trp Tyr Leu Arg
                485                 490                 495

Thr Lys Tyr Gln Gly Ile Cys Pro Pro Val Thr Arg Asn Glu Thr His
            500                 505                 510

Phe Asp Ala Gly Ala Lys Phe His Val Pro Asn Val Thr Pro Tyr Ile
        515                 520                 525

Arg Tyr Phe Val Ser Phe Val Leu Gln Phe Gln Phe His Glu Ala Leu
    530                 535                 540

Cys Lys Glu Ala Gly Tyr Glu Gly Pro Leu His Gln Cys Asp Ile Tyr
545                 550                 555                 560

Arg Ser Thr Lys Ala Gly Ala Lys Leu Arg Lys Val Leu Gln Ala Gly
                565                 570                 575

Ser Ser Arg Pro Trp Gln Glu Val Leu Lys Asp Met Val Gly Leu Asp
            580                 585                 590

Ala Leu Asp Ala Gln Pro Leu Leu Lys Tyr Phe Gln Pro Val Thr Gln
        595                 600                 605

Trp Leu Gln Glu Gln Asn Gln Gln Asn Gly Glu Val Leu Gly Trp Pro
    610                 615                 620

Glu Tyr Gln Trp His Pro Pro Leu Pro Asp Asn Tyr Pro Glu Gly Ile
625                 630                 635                 640

Asp Leu Val Thr Asp Glu Ala Glu Ala Ser Lys Phe Val Glu Glu Tyr
                645                 650                 655

Asp Arg Thr Ser Gln Val Val Trp Asn Glu Tyr Ala Gln Ala Asn Trp
            660                 665                 670

Asn Tyr Asn Thr Asn Ile Thr Thr Glu Thr Ser Lys Ile Leu Leu Gln
        675                 680                 685

Lys Asn Met Gln Ile Ala Asn His Thr Leu Lys Tyr Gly Thr Gln Ala
    690                 695                 700

Arg Lys Phe Asp Val Asn Gln Leu Gln Asn Thr Thr Ile Lys Arg Ile
705                 710                 715                 720

Ile Lys Lys Val Gln Asp Leu Glu Arg Ala Ala Leu Pro Ala Gln Glu
                725                 730                 735
```

```
Leu Glu Glu Tyr Asn Lys Ile Leu Leu Asp Met Glu Thr Thr Tyr Ser
            740                 745                 750

Val Ala Thr Val Cys His Pro Asn Gly Ser Cys Leu Gln Leu Glu Pro
        755                 760                 765

Asp Leu Thr Asn Val Met Ala Thr Ser Arg Lys Tyr Glu Asp Leu Leu
    770                 775                 780

Trp Ala Trp Glu Gly Trp Arg Asp Lys Ala Gly Arg Ala Ile Leu Gln
785                 790                 795                 800

Phe Tyr Pro Lys Tyr Val Glu Leu Ile Asn Gln Ala Ala Arg Leu Asn
                805                 810                 815

Gly Tyr Val Asp Ala Gly Asp Ser Trp Arg Ser Met Tyr Glu Thr Pro
            820                 825                 830

Ser Leu Glu Gln Asp Leu Glu Arg Leu Phe Gln Glu Leu Gln Pro Leu
        835                 840                 845

Tyr Leu Asn Leu His Ala Tyr Val Arg Arg Ala Leu His Arg His Tyr
    850                 855                 860

Gly Ala Gln His Ile Asn Leu Glu Gly Pro Ile Pro Ala His Leu Leu
865                 870                 875                 880

Gly Asn Met Trp Ala Gln Thr Trp Ser Asn Ile Tyr Asp Leu Val Val
                885                 890                 895

Pro Phe Pro Ser Ala Pro Ser Met Asp Thr Thr Glu Ala Met Leu Lys
            900                 905                 910

Gln Gly Trp Thr Pro Arg Arg Met Phe Lys Glu Ala Asp Asp Phe Phe
        915                 920                 925

Thr Ser Leu Gly Leu Leu Pro Val Pro Pro Glu Phe Trp Asn Lys Ser
    930                 935                 940

Met Leu Glu Lys Pro Thr Asp Gly Arg Glu Val Val Cys His Ala Ser
945                 950                 955                 960

Ala Trp Asp Phe Tyr Asn Gly Lys Asp Phe Arg Ile Lys Gln Cys Thr
                965                 970                 975

Thr Val Asn Leu Glu Asp Leu Val Val Ala His His Glu Met Gly His
            980                 985                 990

Ile Gln Tyr Phe Met Gln Tyr Lys  Asp Leu Pro Val Ala  Leu Arg Glu
        995                 1000                1005

Gly Ala  Asn Pro Gly Phe His  Glu Ala Ile Gly Asp  Val Leu Ala
    1010                1015                1020

Leu Ser  Val Ser Thr Pro Lys  His Leu His Ser Leu  Asn Leu Leu
    1025                1030                1035

Ser Ser  Glu Gly Gly Ser Asp  Glu His Asp Ile Asn  Phe Leu Met
```



```
    1040                1045                1050

Lys Met  Ala Leu Asp Lys Ile  Ala Phe Ile Pro Phe  Ser Tyr Leu
    1055                1060                1065

Val Asp  Gln Trp Arg Trp Arg  Val Phe Asp Gly Ser  Ile Thr Lys
    1070                1075                1080

Glu Asn  Tyr Asn Gln Glu Trp  Trp Ser Leu Arg Leu  Lys Tyr Gln
    1085                1090                1095

Gly Leu  Cys Pro Pro Val Pro  Arg Thr Gln Gly Asp  Phe Asp Pro
    1100                1105                1110

Gly Ala  Lys Phe His Ile Pro  Ser Ser Val Pro Tyr  Ile Arg Tyr
    1115                1120                1125

Phe Val  Ser Phe Ile Ile Gln  Phe Gln Phe His Glu  Ala Leu Cys
    1130                1135                1140

Gln Ala  Ala Gly His Thr Gly  Pro Leu His Lys Cys  Asp Ile Tyr
    1145                1150                1155

Gln Ser  Lys Glu Ala Gly Gln  Arg Leu Ala Thr Ala  Met Lys Leu
    1160                1165                1170

Gly Phe  Ser Arg Pro Trp Pro  Glu Ala Met Gln Leu  Ile Thr Gly
    1175                1180                1185

Gln Pro  Asn Met Ser Ala Ser  Ala Met Leu Ser Tyr  Phe Lys Pro
    1190                1195                1200

Leu Leu  Asp Trp Leu Arg Thr  Glu Asn Glu Leu His  Gly Glu Lys
    1205                1210                1215

Leu Gly  Trp Pro Gln Tyr Asn  Trp Thr Pro Asn Ser  Ala Arg Ser
    1220                1225                1230

Glu Gly  Pro Leu Pro Asp Ser  Gly Arg Val Ser Phe  Leu Gly Leu
    1235                1240                1245

Asp Leu  Asp Ala Gln Gln Ala  Arg Val Gly Gln Trp  Leu Leu Leu
    1250                1255                1260

Phe Leu  Gly Ile Ala Leu Leu  Val Ala Thr Leu Gly  Leu Ser Gln
    1265                1270                1275

Arg Leu  Phe Ser Ile Arg His  Arg Ser Leu His Arg  His Ser His
    1280                1285                1290

Gly Pro  Gln Phe Gly Ser Glu  Val Glu Leu Arg His  Ser
    1295                1300                1305
```

<210> 189
<211> 1461
<212> PRT
<213> Homo sapiens

<400> 189

```
Met Ala Ala Glu Arg Gly Ala Arg Arg Leu Leu Ser Thr Pro Ser Phe
```

```
1               5                   10                  15

Trp Leu Tyr Cys Leu Leu Leu Leu Gly Arg Arg Ala Pro Gly Ala Ala
            20                  25                  30

Ala Ala Arg Ser Gly Ser Ala Pro Gln Ser Pro Gly Ala Ser Ile Arg
        35                  40                  45

Thr Phe Thr Pro Phe Tyr Phe Leu Val Glu Pro Val Asp Thr Leu Ser
    50                  55                  60

Val Arg Gly Ser Ser Val Ile Leu Asn Cys Ser Ala Tyr Ser Glu Pro
65                  70                  75                  80

Ser Pro Lys Ile Glu Trp Lys Lys Asp Gly Thr Phe Leu Asn Leu Val
                85                  90                  95

Ser Asp Asp Arg Arg Gln Leu Leu Pro Asp Gly Ser Leu Phe Ile Ser
            100                 105                 110

Asn Val Val His Ser Lys His Asn Lys Pro Asp Glu Gly Tyr Tyr Gln
        115                 120                 125

Cys Val Ala Thr Val Glu Ser Leu Gly Thr Ile Ile Ser Arg Thr Ala
    130                 135                 140

Lys Leu Ile Val Ala Gly Leu Pro Arg Phe Thr Ser Gln Pro Glu Pro
145                 150                 155                 160

Ser Ser Val Tyr Ala Gly Asn Gly Ala Ile Leu Asn Cys Glu Val Asn
                165                 170                 175

Ala Asp Leu Val Pro Phe Val Arg Trp Glu Gln Asn Arg Gln Pro Leu
            180                 185                 190

Leu Leu Asp Asp Arg Val Ile Lys Leu Pro Ser Gly Met Leu Val Ile
        195                 200                 205

Ser Asn Ala Thr Glu Gly Asp Gly Gly Leu Tyr Arg Cys Val Val Glu
    210                 215                 220

Ser Gly Gly Pro Pro Lys Tyr Ser Asp Glu Val Glu Leu Lys Val Leu
225                 230                 235                 240

Pro Asp Pro Glu Val Ile Ser Asp Leu Val Phe Leu Lys Gln Pro Ser
                245                 250                 255

Pro Leu Val Arg Val Ile Gly Gln Asp Val Val Leu Pro Cys Val Ala
            260                 265                 270

Ser Gly Leu Pro Thr Pro Thr Ile Lys Trp Met Lys Asn Glu Glu Ala
        275                 280                 285

Leu Asp Thr Glu Ser Ser Glu Arg Leu Val Leu Leu Ala Gly Gly Ser
    290                 295                 300

Leu Glu Ile Ser Asp Val Thr Glu Asp Asp Ala Gly Thr Tyr Phe Cys
305                 310                 315                 320
```



```
Ile Ala Asp Asn Gly Asn Glu Thr Ile Glu Ala Gln Ala Glu Leu Thr
            325                 330                 335

Val Gln Ala Gln Pro Glu Phe Leu Lys Gln Pro Thr Asn Ile Tyr Ala
        340                 345                 350

His Glu Ser Met Asp Ile Val Phe Glu Cys Glu Val Thr Gly Lys Pro
    355                 360                 365

Thr Pro Thr Val Lys Trp Val Lys Asn Gly Asp Met Val Ile Pro Ser
370                 375                 380

Asp Tyr Phe Lys Ile Val Lys Glu His Asn Leu Gln Val Leu Gly Leu
385                 390                 395                 400

Val Lys Ser Asp Glu Gly Phe Tyr Gln Cys Ile Ala Glu Asn Asp Val
                405                 410                 415

Gly Asn Ala Gln Ala Gly Ala Gln Leu Ile Ile Leu Glu His Ala Pro
            420                 425                 430

Ala Thr Thr Gly Pro Leu Pro Ser Ala Pro Arg Asp Val Val Ala Ser
        435                 440                 445

Leu Val Ser Thr Arg Phe Ile Lys Leu Thr Trp Arg Thr Pro Ala Ser
    450                 455                 460

Asp Pro His Gly Asp Asn Leu Thr Tyr Ser Val Phe Tyr Thr Lys Glu
465                 470                 475                 480

Gly Ile Ala Arg Glu Arg Val Glu Asn Thr Ser His Pro Gly Glu Met
                485                 490                 495

Gln Val Thr Ile Gln Asn Leu Met Pro Ala Thr Val Tyr Ile Phe Arg
            500                 505                 510

Val Met Ala Gln Asn Lys His Gly Ser Gly Glu Ser Ser Ala Pro Leu
        515                 520                 525

Arg Val Glu Thr Gln Pro Glu Val Gln Leu Pro Gly Pro Ala Pro Asn
    530                 535                 540

Leu Arg Ala Tyr Ala Ala Ser Pro Thr Ser Ile Thr Val Thr Trp Glu
545                 550                 555                 560

Thr Pro Val Ser Gly Asn Gly Glu Ile Gln Asn Tyr Lys Leu Tyr Tyr
                565                 570                 575

Met Glu Lys Gly Thr Asp Lys Glu Gln Asp Val Asp Val Ser Ser His
            580                 585                 590

Ser Tyr Thr Ile Asn Gly Leu Lys Lys Tyr Thr Glu Tyr Ser Phe Arg
        595                 600                 605

Val Val Ala Tyr Asn Lys His Gly Pro Gly Val Ser Thr Pro Asp Val
    610                 615                 620

Ala Val Arg Thr Leu Ser Asp Val Pro Ser Ala Ala Pro Gln Asn Leu
625                 630                 635                 640
```

```
Ser Leu Glu Val Arg Asn Ser Lys Ser Ile Met Ile His Trp Gln Pro
                645                 650                 655

Pro Ala Pro Ala Thr Gln Asn Gly Gln Ile Thr Gly Tyr Lys Ile Arg
            660                 665                 670

Tyr Arg Lys Ala Ser Arg Lys Ser Asp Val Thr Glu Thr Leu Val Ser
        675                 680                 685

Gly Thr Gln Leu Ser Gln Leu Ile Glu Gly Leu Asp Arg Gly Thr Glu
    690                 695                 700

Tyr Asn Phe Arg Val Ala Ala Leu Thr Ile Asn Gly Thr Gly Pro Ala
705                 710                 715                 720

Thr Asp Trp Leu Ser Ala Glu Thr Phe Glu Ser Asp Leu Asp Glu Thr
                725                 730                 735

Arg Val Pro Glu Val Pro Ser Ser Leu His Val Arg Pro Leu Val Thr
            740                 745                 750

Ser Ile Val Val Ser Trp Thr Pro Pro Glu Asn Gln Asn Ile Val Val
        755                 760                 765

Arg Gly Tyr Ala Ile Gly Tyr Gly Ile Gly Ser Pro His Ala Gln Thr
    770                 775                 780

Ile Lys Val Asp Tyr Lys Gln Arg Tyr Tyr Thr Ile Glu Asn Leu Asp
785                 790                 795                 800

Pro Ser Ser His Tyr Val Ile Thr Leu Lys Ala Phe Asn Asn Val Gly
                805                 810                 815

Glu Gly Ile Pro Leu Tyr Glu Ser Ala Val Thr Arg Pro His Thr Asp
            820                 825                 830

Thr Ser Glu Val Asp Leu Phe Val Ile Asn Ala Pro Tyr Thr Pro Val
        835                 840                 845

Pro Asp Pro Thr Pro Met Met Pro Pro Val Gly Val Gln Ala Ser Ile
    850                 855                 860

Leu Ser His Asp Thr Ile Arg Ile Thr Trp Ala Asp Asn Ser Leu Pro
865                 870                 875                 880

Lys His Gln Lys Ile Thr Asp Ser Arg Tyr Tyr Thr Val Arg Trp Lys
                885                 890                 895

Thr Asn Ile Pro Ala Asn Thr Lys Tyr Lys Asn Ala Asn Ala Thr Thr
            900                 905                 910

Leu Ser Tyr Leu Val Thr Gly Leu Lys Pro Asn Thr Leu Tyr Glu Phe
        915                 920                 925

Ser Val Met Val Thr Lys Gly Arg Arg Ser Ser Thr Trp Ser Met Thr
    930                 935                 940

Ala His Gly Thr Thr Phe Glu Leu Val Pro Thr Ser Pro Pro Lys Asp
945                 950                 955                 960
```



```
Val Thr Val Val Ser Lys Glu Gly Lys Pro Lys Thr Ile Ile Val Asn
                965                 970                 975

Trp Gln Pro Pro Ser Glu Ala Asn Gly Lys Ile Thr Gly Tyr Ile Ile
            980                 985                 990

Tyr Tyr Ser Thr Asp Val Asn Ala  Glu Ile His Asp Trp  Val Ile Glu
        995                 1000                1005

Pro Val  Val Gly Asn Arg Leu  Thr His Gln Ile Gln  Glu Leu Thr
    1010                1015                1020

Leu Asp  Thr Pro Tyr Tyr Phe  Lys Ile Gln Ala Arg  Asn Ser Lys
    1025                1030                1035

Gly Met  Gly Pro Met Ser Glu  Ala Val Gln Phe Arg  Thr Pro Lys
    1040                1045                1050

Ala Asp  Ser Ser Asp Lys Met  Pro Asn Asp Gln Ala  Ser Gly Ser
    1055                1060                1065

Gly Gly  Lys Gly Ser Arg Leu  Pro Asp Leu Gly Ser  Asp Tyr Lys
    1070                1075                1080

Pro Pro  Met Ser Gly Ser Asn  Ser Pro His Gly Ser  Pro Thr Ser
    1085                1090                1095

Pro Leu  Asp Ser Asn Met Leu  Leu Val Ile Ile Val  Ser Val Gly
    1100                1105                1110

Val Ile  Thr Ile Val Val Val  Val Ile Ile Ala Val  Phe Cys Thr
    1115                1120                1125

Arg Arg  Thr Thr Ser His Gln  Lys Lys Lys Arg Ala  Ala Cys Lys
    1130                1135                1140

Ser Val  Asn Gly Ser His Lys  Tyr Lys Gly Asn Ser  Lys Asp Val
    1145                1150                1155

Lys Pro  Pro Asp Leu Trp Ile  His His Glu Arg Leu  Glu Leu Lys
    1160                1165                1170

Pro Ile  Asp Lys Ser Pro Asp  Pro Asn Pro Ile Met  Thr Asp Thr
    1175                1180                1185

Pro Ile  Pro Arg Asn Ser Gln  Asp Ile Thr Pro Val  Asp Asn Ser
    1190                1195                1200

Met Asp  Ser Asn Ile His Gln  Arg Arg Asn Ser Tyr  Arg Gly His
    1205                1210                1215

Glu Ser  Glu Asp Ser Met Ser  Thr Leu Ala Gly Arg  Arg Gly Met
    1220                1225                1230

Arg Pro  Lys Met Met Met Pro  Phe Asp Ser Gln Pro  Pro Gln Pro
    1235                1240                1245

Val Ile  Ser Ala His Pro Ile  His Ser Leu Asp Asn  Pro His His
```

1250 1255 1260

His Phe His Ser Ser Ser Leu Ala Ser Pro Ala Arg Ser His Leu
1265 1270 1275

Tyr His Pro Gly Ser Pro Trp Pro Ile Gly Thr Ser Met Ser Leu
1280 1285 1290

Ser Asp Arg Ala Asn Ser Thr Glu Ser Val Arg Asn Thr Pro Ser
1295 1300 1305

Thr Asp Thr Met Pro Ala Ser Ser Ser Gln Thr Cys Cys Thr Asp
1310 1315 1320

His Gln Asp Pro Glu Gly Ala Thr Ser Ser Ser Tyr Leu Ala Ser
1325 1330 1335

Ser Gln Glu Glu Asp Ser Gly Gln Ser Leu Pro Thr Ala His Val
1340 1345 1350

Arg Pro Ser His Pro Leu Lys Ser Phe Ala Val Pro Ala Ile Pro
1355 1360 1365

Pro Pro Gly Pro Pro Thr Tyr Asp Pro Ala Leu Pro Ser Thr Pro
1370 1375 1380

Leu Leu Ser Gln Gln Ala Leu Asn His His Ile His Ser Val Lys
1385 1390 1395

Thr Ala Ser Ile Gly Thr Leu Gly Arg Ser Arg Pro Pro Met Pro
1400 1405 1410

Val Val Val Pro Ser Ala Pro Glu Val Gln Glu Thr Thr Arg Met
1415 1420 1425

Leu Glu Asp Ser Glu Ser Ser Tyr Glu Pro Asp Glu Leu Thr Lys
1430 1435 1440

Glu Met Ala His Leu Glu Gly Leu Met Lys Asp Leu Asn Ala Ile
1445 1450 1455

Thr Thr Ala
1460

<210> 190
<211> 736
<212> PRT
<213> Homo sapiens

<400> 190

Met Val Val Thr Arg Ser Ala Arg Ala Lys Ala Ser Ile Gln Ala Ala
1 5 10 15

Ser Ala Glu Ser Ser Gly Gln Lys Ser Phe Ala Ala Asn Gly Ile Gln
20 25 30

Ala His Pro Glu Ser Ser Thr Gly Ser Asp Ala Arg Thr Thr Asp Glu
35 40 45

Ser Gln Thr Thr Gly Lys Gln Ser Leu Ile Pro Arg Thr Pro Lys Ala

50 55 60

Arg Lys Ser Lys Ser Arg Thr Thr Gly Ser Leu Pro Lys Gly Thr Glu
65 70 75 80

Pro Ser Thr Asp Gly Glu Thr Ser Glu Ala Glu Ser Asn Tyr Ser Val
85 90 95

Ser Glu His His Asp Thr Ile Leu Arg Val Thr Arg Arg Arg Gln Ile
100 105 110

Leu Ile Ala Cys Ser Pro Val Ser Ser Val Arg Lys Lys Pro Lys Val
115 120 125

Thr Pro Thr Lys Glu Ser Tyr Thr Glu Glu Ile Val Ser Glu Ala Glu
130 135 140

Ser His Val Ser Gly Ile Ser Arg Ile Val Leu Pro Thr Glu Lys Thr
145 150 155 160

Thr Gly Ala Arg Arg Ser Lys Ala Lys Ser Leu Thr Asp Pro Ser Gln
165 170 175

Glu Ser His Thr Glu Ala Ile Ser Asp Ala Glu Thr Ser Ser Ser Asp
180 185 190

Ile Ser Phe Ser Gly Ile Ala Thr Arg Arg Thr Arg Ser Met Gln Arg
195 200 205

Lys Leu Lys Ala Gln Thr Glu Lys Lys Asp Ser Lys Ile Val Pro Gly
210 215 220

Asn Glu Lys Gln Ile Val Gly Thr Pro Val Asn Ser Glu Asp Ser Asp
225 230 235 240

Thr Arg Gln Thr Ser His Leu Gln Ala Arg Ser Leu Ser Glu Ile Asn
245 250 255

Lys Pro Asn Phe Tyr Asn Asn Asp Phe Asp Asp Asp Phe Ser His Arg
260 265 270

Ser Ser Glu Asn Ile Leu Thr Val His Glu Gln Ala Asn Val Glu Ser
275 280 285

Leu Lys Glu Thr Lys Gln Asn Cys Lys Asp Leu Asp Glu Asp Ala Asn
290 295 300

Gly Ile Thr Asp Glu Gly Lys Glu Ile Asn Glu Lys Ser Ser Gln Leu
305 310 315 320

Lys Asn Leu Ser Glu Leu Gln Asp Thr Ser Leu Gln Gln Leu Val Ser
325 330 335

Gln Arg His Ser Thr Pro Gln Asn Lys Asn Ala Val Ser Val His Ser
340 345 350

Asn Leu Asn Ser Glu Ala Val Met Lys Ser Leu Thr Gln Thr Phe Ala
355 360 365

```
Thr Val Glu Val Gly Arg Trp Asn Asn Asn Lys Lys Ser Pro Ile Lys
    370                 375                 380

Ala Ser Asp Leu Thr Lys Phe Gly Asp Cys Gly Gly Ser Asp Asp Glu
385                 390                 395                 400

Glu Glu Ser Thr Val Ile Ser Val Ser Glu Asp Met Asn Ser Glu Gly
                405                 410                 415

Asn Val Asp Phe Glu Cys Asp Thr Lys Leu Tyr Thr Ser Ala Pro Asn
            420                 425                 430

Thr Ser Gln Gly Lys Asp Asn Ser Val Leu Leu Val Leu Ser Ser Asp
        435                 440                 445

Glu Ser Gln Gln Ser Glu Asn Ser Glu Asn Glu Glu Asp Thr Leu Cys
    450                 455                 460

Phe Val Glu Asn Ser Gly Gln Arg Glu Ser Leu Ser Gly Asp Thr Gly
465                 470                 475                 480

Ser Leu Ser Cys Asp Asn Ala Leu Phe Val Ile Asp Thr Thr Pro Gly
                485                 490                 495

Met Ser Ala Asp Lys Asn Phe Tyr Leu Glu Glu Glu Asp Lys Ala Ser
            500                 505                 510

Glu Val Ala Ile Glu Glu Glu Lys Glu Glu Glu Glu Asp Glu Lys Ser
        515                 520                 525

Glu Glu Asp Ser Ser Asp His Asp Glu Asn Glu Asp Glu Phe Ser Asp
    530                 535                 540

Glu Glu Asp Phe Leu Asn Ser Thr Lys Ala Lys Leu Leu Lys Leu Thr
545                 550                 555                 560

Ser Ser Ser Ile Asp Pro Gly Leu Ser Ile Lys Gln Leu Gly Gly Leu
                565                 570                 575

Tyr Ile Asn Phe Asn Ala Asp Lys Leu Gln Ser Asn Lys Arg Thr Leu
            580                 585                 590

Thr Gln Ile Lys Glu Lys Lys Lys Asn Glu Leu Leu Gln Lys Ala Val
        595                 600                 605

Ile Thr Pro Asp Phe Glu Lys Asn His Cys Val Pro Pro Tyr Ser Glu
    610                 615                 620

Ser Lys Tyr Gln Leu Gln Lys Lys Arg Arg Lys Glu Arg Gln Lys Thr
625                 630                 635                 640

Ala Gly Asp Gly Trp Phe Gly Met Lys Ala Pro Glu Met Thr Asn Glu
                645                 650                 655

Leu Lys Asn Asp Leu Lys Ala Leu Lys Met Arg Ala Ser Met Asp Pro
            660                 665                 670

Lys Arg Phe Tyr Lys Lys Asn Asp Arg Asp Gly Phe Pro Lys Tyr Phe
        675                 680                 685
```



```
Gln Ile Gly Thr Ile Val Asp Asn Pro Ala Asp Phe Tyr His Ser Arg
    690                 695                 700

Ile Pro Lys Lys Gln Arg Lys Arg Thr Ile Val Glu Asp Cys Trp Leu
705                 710                 715                 720

Ile Leu Asn Ser Glu Ile Gln Pro Lys Glu Val Leu Arg Asp His Gly
                725                 730                 735
```

<210> 191
<211> 465
<212> PRT
<213> Homo sapiens

<400> 191

```
Met Ala Met Thr Gly Ser Thr Pro Cys Ser Ser Met Ser Asn His Thr
1               5                   10                  15

Lys Glu Arg Val Thr Met Thr Lys Val Thr Leu Glu Asn Phe Tyr Ser
            20                  25                  30

Asn Leu Ile Ala Gln His Glu Glu Arg Glu Met Arg Gln Lys Lys Leu
        35                  40                  45

Glu Lys Val Met Glu Glu Glu Gly Leu Lys Asp Glu Glu Lys Arg Leu
    50                  55                  60

Arg Arg Ser Ala His Ala Arg Lys Glu Thr Glu Phe Leu Arg Leu Lys
65                  70                  75                  80

Arg Thr Arg Leu Gly Leu Glu Asp Phe Glu Ser Leu Lys Val Ile Gly
                85                  90                  95

Arg Gly Ala Phe Gly Glu Val Arg Leu Val Gln Lys Lys Asp Thr Gly
            100                 105                 110

His Val Tyr Ala Met Lys Ile Leu Arg Lys Ala Asp Met Leu Glu Lys
        115                 120                 125

Glu Gln Val Gly His Ile Arg Ala Glu Arg Asp Ile Leu Val Glu Ala
    130                 135                 140

Asp Ser Leu Trp Val Val Lys Met Phe Tyr Ser Phe Gln Asp Lys Leu
145                 150                 155                 160

Asn Leu Tyr Leu Ile Met Glu Phe Leu Pro Gly Gly Asp Met Met Thr
                165                 170                 175

Leu Leu Met Lys Lys Asp Thr Leu Thr Glu Glu Glu Thr Gln Phe Tyr
            180                 185                 190

Ile Ala Glu Thr Val Leu Ala Ile Asp Ser Ile His Gln Leu Gly Phe
        195                 200                 205

Ile His Arg Asp Ile Lys Pro Asp Asn Leu Leu Leu Asp Ser Lys Gly
    210                 215                 220

His Val Lys Leu Ser Asp Phe Gly Leu Cys Thr Gly Leu Lys Lys Ala
225                 230                 235                 240
```

His Arg Thr Glu Phe Tyr Arg Asn Leu Asn His Ser Leu Pro Ser Asp
245 250 255

Phe Thr Phe Gln Asn Met Asn Ser Lys Arg Lys Ala Glu Thr Trp Lys
260 265 270

Arg Asn Arg Arg Gln Leu Ala Phe Ser Thr Val Gly Thr Pro Asp Tyr
275 280 285

Ile Ala Pro Glu Val Phe Met Gln Thr Gly Tyr Asn Lys Leu Cys Asp
290 295 300

Trp Trp Ser Leu Gly Val Ile Met Tyr Glu Met Leu Ile Gly Tyr Pro
305 310 315 320

Pro Phe Cys Ser Glu Thr Pro Gln Glu Thr Tyr Lys Lys Val Met Asn
325 330 335

Trp Lys Glu Thr Leu Thr Phe Pro Pro Glu Val Pro Ile Ser Glu Lys
340 345 350

Ala Lys Asp Leu Ile Leu Arg Phe Cys Cys Glu Trp Glu His Arg Ile
355 360 365

Gly Ala Pro Gly Val Glu Glu Ile Lys Ser Asn Ser Phe Phe Glu Gly
370 375 380

Val Asp Trp Glu His Ile Arg Glu Arg Pro Ala Ala Ile Ser Ile Glu
385 390 395 400

Ile Lys Ser Ile Asp Asp Thr Ser Asn Phe Asp Glu Phe Pro Glu Ser
405 410 415

Asp Ile Leu Lys Pro Thr Val Ala Thr Ser Asn His Pro Glu Thr Asp
420 425 430

Tyr Lys Asn Lys Asp Trp Val Phe Ile Asn Tyr Thr Tyr Lys Arg Phe
435 440 445

Glu Gly Leu Thr Ala Arg Gly Ala Ile Pro Ser Tyr Met Lys Ala Ala
450 455 460

Lys
465

<210> 192
<211> 73
<212> PRT
<213> Homo sapiens

<400> 192

Met Thr Tyr Phe Pro Leu Gly Arg Tyr Pro Val Val Gly Leu Leu Asp
1 5 10 15

Gln Met Val Val Leu Ser Thr Phe Ser Ser Leu Lys Asn Leu His Ile
20 25 30

Val Phe His Ser Gly Cys Thr Ser Leu His Ser His Gln Leu Cys Lys
35 40 45

Arg Val Pro Phe Ser Pro His Pro Arg Gln His Leu Leu Phe Phe Asp
50 55 60

Phe Trp Ile Lys Ala Ile Leu Ala Glu
65 70

<210> 193
<211> 410
<212> PRT
<213> Homo sapiens

<400> 193

Met Val Cys Phe Arg Leu Phe Pro Val Pro Gly Ser Gly Leu Val Leu
1 5 10 15

Val Cys Leu Val Leu Gly Ala Val Arg Ser Tyr Ala Leu Glu Leu Asn
20 25 30

Leu Thr Asp Ser Glu Asn Ala Thr Cys Leu Tyr Ala Lys Trp Gln Met
35 40 45

Asn Phe Thr Val Arg Tyr Glu Thr Thr Asn Lys Thr Tyr Lys Thr Val
50 55 60

Thr Ile Ser Asp His Gly Thr Val Thr Tyr Asn Gly Ser Ile Cys Gly
65 70 75 80

Asp Asp Gln Asn Gly Pro Lys Ile Ala Val Gln Phe Gly Pro Gly Phe
85 90 95

Ser Trp Ile Ala Asn Phe Thr Lys Ala Ala Ser Thr Tyr Ser Ile Asp
100 105 110

Ser Val Ser Phe Ser Tyr Asn Thr Gly Asp Asn Thr Thr Phe Pro Asp
115 120 125

Ala Glu Asp Lys Gly Ile Leu Thr Val Asp Glu Leu Leu Ala Ile Arg
130 135 140

Ile Pro Leu Asn Asp Leu Phe Arg Cys Asn Ser Leu Ser Thr Leu Glu
145 150 155 160

Lys Asn Asp Val Val Gln His Tyr Trp Asp Val Leu Val Gln Ala Phe
165 170 175

Val Gln Asn Gly Thr Val Ser Thr Asn Glu Phe Leu Cys Asp Lys Asp
180 185 190

Lys Thr Ser Thr Val Ala Pro Thr Ile His Thr Thr Val Pro Ser Pro
195 200 205

Thr Thr Thr Pro Thr Pro Lys Glu Lys Pro Glu Ala Gly Thr Tyr Ser
210 215 220

Val Asn Asn Gly Asn Asp Thr Cys Leu Leu Ala Thr Met Gly Leu Gln
225 230 235 240

Leu Asn Ile Thr Gln Asp Lys Val Ala Ser Val Ile Asn Ile Asn Pro
245 250 255

Asn Thr Thr His Ser Thr Gly Ser Cys Arg Ser His Thr Ala Leu Leu
260 265 270

Arg Leu Asn Ser Ser Thr Ile Lys Tyr Leu Asp Phe Val Phe Ala Val
275 280 285

Lys Asn Glu Asn Arg Phe Tyr Leu Lys Glu Val Asn Ile Ser Met Tyr
290 295 300

Leu Val Asn Gly Ser Val Phe Ser Ile Ala Asn Asn Asn Leu Ser Tyr
305 310 315 320

Trp Asp Ala Pro Leu Gly Ser Ser Tyr Met Cys Asn Lys Glu Gln Thr
325 330 335

Val Ser Val Ser Gly Ala Phe Gln Ile Asn Thr Phe Asp Leu Arg Val
340 345 350

Gln Pro Phe Asn Val Thr Gln Gly Lys Tyr Ser Thr Ala Gln Glu Cys
355 360 365

Ser Leu Asp Asp Asp Thr Ile Leu Ile Pro Ile Ile Val Gly Ala Gly
370 375 380

Leu Ser Gly Leu Ile Ile Val Ile Val Ile Ala Tyr Val Ile Gly Arg
385 390 395 400

Arg Lys Ser Tyr Ala Gly Tyr Gln Thr Leu
405 410

<210> 194
<211> 480
<212> PRT
<213> Homo sapiens

<400> 194

Met Ala Gly Gly Gly Gly Asp Leu Ser Thr Arg Arg Leu Asn Glu Cys
1 5 10 15

Ile Ser Pro Val Ala Asn Glu Met Asn His Leu Pro Ala His Ser His
20 25 30

Asp Leu Gln Arg Met Phe Thr Glu Asp Gln Gly Val Asp Asp Arg Leu
35 40 45

Leu Tyr Asp Ile Val Phe Lys His Phe Lys Arg Asn Lys Val Glu Ile
50 55 60

Ser Asn Ala Ile Lys Lys Thr Phe Pro Phe Leu Glu Gly Leu Arg Asp
65 70 75 80

Arg Asp Leu Ile Thr Asn Lys Met Phe Glu Asp Ser Gln Asp Ser Cys
85 90 95

Arg Asn Leu Val Pro Val Gln Arg Val Val Tyr Asn Val Leu Ser Glu
100 105 110

Leu Glu Lys Thr Phe Asn Leu Pro Val Leu Glu Ala Leu Phe Ser Asp
115 120 125

Val Asn Met Gln Glu Tyr Pro Asp Leu Ile His Ile Tyr Lys Gly Phe
130 135 140

Glu Asn Val Ile His Asp Lys Leu Pro Leu Gln Glu Ser Glu Glu Glu
145 150 155 160

Glu Arg Glu Glu Arg Ser Gly Leu Gln Leu Ser Leu Glu Gln Gly Thr
165 170 175

Gly Glu Asn Ser Phe Arg Ser Leu Thr Trp Pro Pro Ser Gly Ser Pro
180 185 190

Ser His Ala Gly Thr Thr Pro Pro Glu Asn Gly Leu Ser Glu His Pro
195 200 205

Cys Glu Thr Glu Gln Ile Asn Ala Lys Arg Lys Asp Thr Thr Ser Asp
210 215 220

Lys Asp Asp Ser Leu Gly Ser Gln Gln Thr Asn Glu Gln Cys Ala Gln
225 230 235 240

Lys Ala Glu Pro Thr Glu Ser Cys Glu Gln Ile Ala Val Gln Val Asn
245 250 255

Asn Gly Asp Ala Gly Arg Glu Met Pro Cys Pro Leu Pro Cys Asp Glu
260 265 270

Glu Ser Pro Glu Ala Glu Leu His Asn His Gly Ile Gln Ile Asn Ser
275 280 285

Cys Ser Val Arg Leu Val Asp Ile Lys Lys Glu Lys Pro Phe Ser Asn
290 295 300

Ser Lys Val Glu Cys Gln Ala Gln Ala Arg Thr His His Asn Gln Ala
305 310 315 320

Ser Asp Ile Ile Val Ile Ser Ser Glu Asp Ser Glu Gly Ser Thr Asp
325 330 335

Val Asp Glu Pro Leu Glu Val Phe Ile Ser Ala Pro Arg Ser Glu Pro
340 345 350

Val Ile Asn Asn Asp Asn Pro Leu Glu Ser Asn Asp Glu Lys Glu Gly
355 360 365

Gln Glu Ala Thr Cys Ser Arg Pro Gln Ile Val Pro Glu Pro Met Asp
370 375 380

Phe Arg Lys Leu Ser Thr Phe Arg Glu Ser Phe Lys Lys Arg Val Ile
385 390 395 400

Gly Gln Asp His Asp Phe Ser Glu Ser Ser Glu Glu Glu Ala Pro Ala
405 410 415

Glu Ala Ser Ser Gly Ala Leu Arg Ser Lys His Gly Glu Lys Ala Pro
420 425 430

Met Thr Ser Arg Ser Thr Ser Thr Trp Arg Ile Pro Ser Arg Lys Arg
435 440 445

```
Arg Phe Ser Ser Ser Asp Phe Ser Asp Leu Ser Asn Gly Glu Glu Leu
    450                 455                 460

Gln Glu Thr Cys Ser Ser Ser Leu Arg Arg Gly Ser Gly Lys Glu Asp
465                 470                 475                 480
```

<210> 195
<211> 339
<212> PRT
<213> Homo sapiens

<400> 195

```
Met Trp Gln Leu Trp Ala Ser Leu Cys Cys Leu Leu Val Leu Ala Asn
1               5                   10                  15

Ala Arg Ser Arg Pro Ser Phe His Pro Leu Ser Asp Glu Leu Val Asn
            20                  25                  30

Tyr Val Asn Lys Arg Asn Thr Thr Trp Gln Ala Gly His Asn Phe Tyr
        35                  40                  45

Asn Val Asp Met Ser Tyr Leu Lys Arg Leu Cys Gly Thr Phe Leu Gly
    50                  55                  60

Gly Pro Lys Pro Pro Gln Arg Val Met Phe Thr Glu Asp Leu Lys Leu
65                  70                  75                  80

Pro Ala Ser Phe Asp Ala Arg Glu Gln Trp Pro Gln Cys Pro Thr Ile
                85                  90                  95

Lys Glu Ile Arg Asp Gln Gly Ser Cys Gly Ser Cys Trp Ala Phe Gly
            100                 105                 110

Ala Val Glu Ala Ile Ser Asp Arg Ile Cys Ile His Thr Asn Ala His
        115                 120                 125

Val Ser Val Glu Val Ser Ala Glu Asp Leu Leu Thr Cys Cys Gly Ser
    130                 135                 140

Met Cys Gly Asp Gly Cys Asn Gly Gly Tyr Pro Ala Glu Ala Trp Asn
145                 150                 155                 160

Phe Trp Thr Arg Lys Gly Leu Val Ser Gly Gly Leu Tyr Glu Ser His
                165                 170                 175

Val Gly Cys Arg Pro Tyr Ser Ile Pro Pro Cys Glu His His Val Asn
            180                 185                 190

Gly Ser Arg Pro Pro Cys Thr Gly Glu Gly Asp Thr Pro Lys Cys Ser
        195                 200                 205

Lys Ile Cys Glu Pro Gly Tyr Ser Pro Thr Tyr Lys Gln Asp Lys His
    210                 215                 220

Tyr Gly Tyr Asn Ser Tyr Ser Val Ser Asn Ser Glu Lys Asp Ile Met
225                 230                 235                 240

Ala Glu Ile Tyr Lys Asn Gly Pro Val Glu Gly Ala Phe Ser Val Tyr
                245                 250                 255
```



```
Ser Asp Phe Leu Leu Tyr Lys Ser Gly Val Tyr Gln His Val Thr Gly
            260                 265                 270

Glu Met Met Gly Gly His Ala Ile Arg Ile Leu Gly Trp Gly Val Glu
        275                 280                 285

Asn Gly Thr Pro Tyr Trp Leu Val Ala Asn Ser Trp Asn Thr Asp Trp
    290                 295                 300

Gly Asp Asn Gly Phe Phe Lys Ile Leu Arg Gly Gln Asp His Cys Gly
305                 310                 315                 320

Ile Glu Ser Glu Val Val Ala Gly Ile Pro Arg Thr Asp Gln Tyr Trp
                325                 330                 335

Glu Lys Ile
```

<210> 196
<211> 2328
<212> PRT
<213> Homo sapiens

<400> 196

```
Lys Ser Lys Arg Gln Ala Gln Gln Met Val Gln Pro Gln Ser Pro Val
1               5                   10                  15

Ala Val Ser Gln Ser Lys Pro Gly Cys Tyr Asp Asn Gly Lys His Tyr
            20                  25                  30

Gln Ile Asn Gln Gln Trp Glu Arg Thr Tyr Leu Gly Asn Val Leu Val
        35                  40                  45

Cys Thr Cys Tyr Gly Gly Ser Arg Gly Phe Asn Cys Glu Ser Lys Pro
    50                  55                  60

Glu Ala Glu Glu Thr Cys Phe Asp Lys Tyr Thr Gly Asn Thr Tyr Arg
65                  70                  75                  80

Val Gly Asp Thr Tyr Glu Arg Pro Lys Asp Ser Met Ile Trp Asp Cys
                85                  90                  95

Thr Cys Ile Gly Ala Gly Arg Gly Arg Ile Ser Cys Thr Ile Ala Asn
            100                 105                 110

Arg Cys His Glu Gly Gly Gln Ser Tyr Lys Ile Gly Asp Thr Trp Arg
        115                 120                 125

Arg Pro His Glu Thr Gly Gly Tyr Met Leu Glu Cys Val Cys Leu Gly
    130                 135                 140

Asn Gly Lys Gly Glu Trp Thr Cys Lys Pro Ile Ala Glu Lys Cys Phe
145                 150                 155                 160

Asp His Ala Ala Gly Thr Ser Tyr Val Val Gly Glu Thr Trp Glu Lys
                165                 170                 175

Pro Tyr Gln Gly Trp Met Met Val Asp Cys Thr Cys Leu Gly Glu Gly
            180                 185                 190
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```
Ser Gly Arg Ile Thr Cys Thr Ser Arg Asn Arg Cys Asn Asp Gln Asp
        195                 200                 205

Thr Arg Thr Ser Tyr Arg Ile Gly Asp Thr Trp Ser Lys Lys Asp Asn
    210                 215                 220

Arg Gly Asn Leu Leu Gln Cys Ile Cys Thr Gly Asn Gly Arg Gly Glu
225                 230                 235                 240

Trp Lys Cys Glu Arg His Thr Ser Val Gln Thr Thr Ser Ser Gly Ser
                245                 250                 255

Gly Pro Phe Thr Asp Val Arg Ala Ala Val Tyr Gln Pro Gln Pro His
            260                 265                 270

Pro Gln Pro Pro Pro Tyr Gly His Cys Val Thr Asp Ser Gly Val Val
        275                 280                 285

Tyr Ser Val Gly Met Gln Trp Leu Lys Thr Gln Gly Asn Lys Gln Met
    290                 295                 300

Leu Cys Thr Cys Leu Gly Asn Gly Val Ser Cys Gln Glu Thr Ala Val
305                 310                 315                 320

Thr Gln Thr Tyr Gly Gly Asn Leu Asn Gly Glu Pro Cys Val Leu Pro
                325                 330                 335

Phe Thr Tyr Asn Gly Arg Thr Phe Tyr Ser Cys Thr Thr Glu Gly Arg
            340                 345                 350

Gln Asp Gly His Leu Trp Cys Ser Thr Thr Ser Asn Tyr Glu Gln Asp
        355                 360                 365

Gln Lys Tyr Ser Phe Cys Thr Asp His Thr Val Leu Val Gln Thr Gln
    370                 375                 380

Gly Gly Asn Ser Asn Gly Ala Leu Cys His Phe Pro Phe Leu Tyr Asn
385                 390                 395                 400

Asn His Asn Tyr Thr Asp Cys Thr Ser Glu Gly Arg Arg Asp Asn Met
                405                 410                 415

Lys Trp Cys Gly Thr Thr Gln Asn Tyr Asp Ala Asp Gln Lys Phe Gly
            420                 425                 430

Phe Cys Pro Met Ala Ala His Glu Glu Ile Cys Thr Thr Asn Glu Gly
        435                 440                 445

Val Met Tyr Arg Ile Gly Asp Gln Trp Asp Lys Gln His Asp Met Gly
    450                 455                 460

His Met Met Arg Cys Thr Cys Val Gly Asn Gly Arg Gly Glu Trp Thr
465                 470                 475                 480

Cys Ile Ala Tyr Ser Gln Leu Arg Asp Gln Cys Ile Val Asp Asp Ile
                485                 490                 495

Thr Tyr Asn Val Asn Asp Thr Phe His Lys Arg His Glu Glu Gly His
```



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            500                 505                 510

Met Leu Asn Cys Thr Cys Phe Gly Gln Gly Arg Gly Arg Trp Lys Cys
        515                 520                 525

Asp Pro Val Asp Gln Cys Gln Asp Ser Glu Thr Gly Thr Phe Tyr Gln
    530                 535                 540

Ile Gly Asp Ser Trp Glu Lys Tyr Val His Gly Val Arg Tyr Gln Cys
545                 550                 555                 560

Tyr Cys Tyr Gly Arg Gly Ile Gly Glu Trp His Cys Gln Pro Leu Gln
                565                 570                 575

Thr Tyr Pro Ser Ser Ser Gly Pro Val Glu Val Phe Ile Thr Glu Thr
            580                 585                 590

Pro Ser Gln Pro Asn Ser His Pro Ile Gln Trp Asn Ala Pro Gln Pro
        595                 600                 605

Ser His Ile Ser Lys Tyr Ile Leu Arg Trp Arg Pro Lys Asn Ser Val
    610                 615                 620

Gly Arg Trp Lys Glu Ala Thr Ile Pro Gly His Leu Asn Ser Tyr Thr
625                 630                 635                 640

Ile Lys Gly Leu Lys Pro Gly Val Val Tyr Glu Gly Gln Leu Ile Ser
                645                 650                 655

Ile Gln Gln Tyr Gly His Gln Glu Val Thr Arg Phe Asp Phe Thr Thr
            660                 665                 670

Thr Ser Thr Ser Thr Pro Val Thr Ser Asn Thr Val Thr Gly Glu Thr
        675                 680                 685

Thr Pro Phe Ser Pro Leu Val Ala Thr Ser Glu Ser Val Thr Glu Ile
    690                 695                 700

Thr Ala Ser Ser Phe Val Val Ser Trp Val Ser Ala Ser Asp Thr Val
705                 710                 715                 720

Ser Gly Phe Arg Val Glu Tyr Glu Leu Ser Glu Glu Gly Asp Glu Pro
                725                 730                 735

Gln Tyr Leu Asp Leu Pro Ser Thr Ala Thr Ser Val Asn Ile Pro Asp
            740                 745                 750

Leu Leu Pro Gly Arg Lys Tyr Ile Val Asn Val Tyr Gln Ile Ser Glu
        755                 760                 765

Asp Gly Glu Gln Ser Leu Ile Leu Ser Thr Ser Gln Thr Thr Ala Pro
    770                 775                 780

Asp Ala Pro Pro Asp Pro Thr Val Asp Gln Val Asp Asp Thr Ser Ile
785                 790                 795                 800

Val Val Arg Trp Ser Arg Pro Gln Ala Pro Ile Thr Gly Tyr Arg Ile
                805                 810                 815
```

Val Tyr Ser Pro Ser Val Glu Gly Ser Ser Thr Glu Leu Asn Leu Pro
820 825 830

Glu Thr Ala Asn Ser Val Thr Leu Ser Asp Leu Gln Pro Gly Val Gln
835 840 845

Tyr Asn Ile Thr Ile Tyr Ala Val Glu Glu Asn Gln Glu Ser Thr Pro
850 855 860

Val Val Ile Gln Gln Glu Thr Thr Gly Thr Pro Arg Ser Asp Thr Val
865 870 875 880

Pro Ser Pro Arg Asp Leu Gln Phe Val Glu Val Thr Asp Val Lys Val
885 890 895

Thr Ile Met Trp Thr Pro Pro Glu Ser Ala Val Thr Gly Tyr Arg Val
900 905 910

Asp Val Ile Pro Val Asn Leu Pro Gly Glu His Gly Gln Arg Leu Pro
915 920 925

Ile Ser Arg Asn Thr Phe Ala Glu Val Thr Gly Leu Ser Pro Gly Val
930 935 940

Thr Tyr Tyr Phe Lys Val Phe Ala Val Ser His Gly Arg Glu Ser Lys
945 950 955 960

Pro Leu Thr Ala Gln Gln Thr Thr Lys Leu Asp Ala Pro Thr Asn Leu
965 970 975

Gln Phe Val Asn Glu Thr Asp Ser Thr Val Leu Val Arg Trp Thr Pro
980 985 990

Pro Arg Ala Gln Ile Thr Gly Tyr Arg Leu Thr Val Gly Leu Thr Arg
995 1000 1005

Arg Gly Gln Pro Arg Gln Tyr Asn Val Gly Pro Ser Val Ser Lys
1010 1015 1020

Tyr Pro Leu Arg Asn Leu Gln Pro Ala Ser Glu Tyr Thr Val Ser
1025 1030 1035

Leu Val Ala Ile Lys Gly Asn Gln Glu Ser Pro Lys Ala Thr Gly
1040 1045 1050

Val Phe Thr Thr Leu Gln Pro Gly Ser Ser Ile Pro Pro Tyr Asn
1055 1060 1065

Thr Glu Val Thr Glu Thr Thr Ile Val Ile Thr Trp Thr Pro Ala
1070 1075 1080

Pro Arg Ile Gly Phe Lys Leu Gly Val Arg Pro Ser Gln Gly Gly
1085 1090 1095

Glu Ala Pro Arg Glu Val Thr Ser Asp Ser Gly Ser Ile Val Val
1100 1105 1110

Ser Gly Leu Thr Pro Gly Val Glu Tyr Val Tyr Thr Ile Gln Val
1115 1120 1125

Leu Arg Asp Gly Gln Glu Arg Asp Ala Pro Ile Val Asn Lys Val
1130 1135 1140

Val Thr Pro Leu Ser Pro Pro Thr Asn Leu His Leu Glu Ala Asn
1145 1150 1155

Pro Asp Thr Gly Val Leu Thr Val Ser Trp Glu Arg Ser Thr Thr
1160 1165 1170

Pro Asp Ile Thr Gly Tyr Arg Ile Thr Thr Thr Pro Thr Asn Gly
1175 1180 1185

Gln Gln Gly Asn Ser Leu Glu Glu Val Val His Ala Asp Gln Ser
1190 1195 1200

Ser Cys Thr Phe Asp Asn Leu Ser Pro Gly Leu Glu Tyr Asn Val
1205 1210 1215

Ser Val Tyr Thr Val Lys Asp Asp Lys Glu Ser Val Pro Ile Ser
1220 1225 1230

Asp Thr Ile Ile Pro Ala Val Pro Pro Pro Thr Asp Leu Arg Phe
1235 1240 1245

Thr Asn Ile Gly Pro Asp Thr Met Arg Val Thr Trp Ala Pro Pro
1250 1255 1260

Pro Ser Ile Asp Leu Thr Asn Phe Leu Val Arg Tyr Ser Pro Val
1265 1270 1275

Lys Asn Glu Glu Asp Val Ala Glu Leu Ser Ile Ser Pro Ser Asp
1280 1285 1290

Asn Ala Val Val Leu Thr Asn Leu Leu Pro Gly Thr Glu Tyr Val
1295 1300 1305

Val Ser Val Ser Ser Val Tyr Glu Gln His Glu Ser Thr Pro Leu
1310 1315 1320

Arg Gly Arg Gln Lys Thr Gly Leu Asp Ser Pro Thr Gly Ile Asp
1325 1330 1335

Phe Ser Asp Ile Thr Ala Asn Ser Phe Thr Val His Trp Ile Ala
1340 1345 1350

Pro Arg Ala Thr Ile Thr Gly Tyr Arg Ile Arg His His Pro Glu
1355 1360 1365

His Phe Ser Gly Arg Pro Arg Glu Asp Arg Val Pro His Ser Arg
1370 1375 1380

Asn Ser Ile Thr Leu Thr Asn Leu Thr Pro Gly Thr Glu Tyr Val
1385 1390 1395

Val Ser Ile Val Ala Leu Asn Gly Arg Glu Glu Ser Pro Leu Leu
1400 1405 1410

Ile Gly Gln Gln Ser Thr Val Ser Asp Val Pro Arg Asp Leu Glu
1415 1420 1425

```
Val Val  Ala Ala Thr Pro Thr  Ser Leu Leu Ile Ser  Trp Asp Ala
1430                 1435                 1440

Pro Ala  Val Thr Val Arg Tyr  Tyr Arg Ile Thr Tyr  Gly Glu Thr
1445                 1450                 1455

Gly Gly  Asn Ser Pro Val Gln  Glu Phe Thr Val Pro  Gly Ser Lys
1460                 1465                 1470

Ser Thr  Ala Thr Ile Ser Gly  Leu Lys Pro Gly Val  Asp Tyr Thr
1475                 1480                 1485

Ile Thr  Val Tyr Ala Val Thr  Gly Arg Gly Asp Ser  Pro Ala Ser
1490                 1495                 1500

Ser Lys  Pro Ile Ser Ile Asn  Tyr Arg Thr Glu Ile  Asp Lys Pro
1505                 1510                 1515

Ser Gln  Met Gln Val Thr Asp  Val Gln Asp Asn Ser  Ile Ser Val
1520                 1525                 1530

Lys Trp  Leu Pro Ser Ser Ser  Pro Val Thr Gly Tyr  Arg Val Thr
1535                 1540                 1545

Thr Thr  Pro Lys Asn Gly Pro  Gly Pro Thr Lys Thr  Lys Thr Ala
1550                 1555                 1560

Gly Pro  Asp Gln Thr Glu Met  Thr Ile Glu Gly Leu  Gln Pro Thr
1565                 1570                 1575

Val Glu  Tyr Val Val Ser Val  Tyr Ala Gln Asn Pro  Ser Gly Glu
1580                 1585                 1590

Ser Gln  Pro Leu Val Gln Thr  Ala Val Thr Asn Ile  Asp Arg Pro
1595                 1600                 1605

Lys Gly  Leu Ala Phe Thr Asp  Val Asp Val Asp Ser  Ile Lys Ile
1610                 1615                 1620

Ala Trp  Glu Ser Pro Gln Gly  Gln Val Ser Arg Tyr  Arg Val Thr
1625                 1630                 1635

Tyr Ser  Ser Pro Glu Asp Gly  Ile His Glu Leu Phe  Pro Ala Pro
1640                 1645                 1650

Asp Gly  Glu Glu Asp Thr Ala  Glu Leu Gln Gly Leu  Arg Pro Gly
1655                 1660                 1665

Ser Glu  Tyr Thr Val Ser Val  Val Ala Leu His Asp  Asp Met Glu
1670                 1675                 1680

Ser Gln  Pro Leu Ile Gly Thr  Gln Ser Thr Ala Ile  Pro Ala Pro
1685                 1690                 1695

Thr Asp  Leu Lys Phe Thr Gln  Val Thr Pro Thr Ser  Leu Ser Ala
1700                 1705                 1710

Gln Trp  Thr Pro Pro Asn Val  Gln Leu Thr Gly Tyr  Arg Val Arg
```



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1715                 1720                 1725

Val Thr  Pro Lys Glu Lys Thr  Gly Pro Met Lys Glu  Ile Asn Leu
1730                 1735                 1740

Ala Pro  Asp Ser Ser Ser Val  Val Val Ser Gly Leu  Met Val Ala
1745                 1750                 1755

Thr Lys  Tyr Glu Val Ser Val  Tyr Ala Leu Lys Asp  Thr Leu Thr
1760                 1765                 1770

Ser Arg  Pro Ala Gln Gly Val  Val Thr Thr Leu Glu  Asn Val Ser
1775                 1780                 1785

Pro Pro  Arg Arg Ala Arg Val  Thr Asp Ala Thr Glu  Thr Thr Ile
1790                 1795                 1800

Thr Ile  Ser Trp Arg Thr Lys  Thr Glu Thr Ile Thr  Gly Phe Gln
1805                 1810                 1815

Val Asp  Ala Val Pro Ala Asn  Gly Gln Thr Pro Ile  Gln Arg Thr
1820                 1825                 1830

Ile Lys  Pro Asp Val Arg Ser  Tyr Thr Ile Thr Gly  Leu Gln Pro
1835                 1840                 1845

Gly Thr  Asp Tyr Lys Ile Tyr  Leu Tyr Thr Leu Asn  Asp Asn Ala
1850                 1855                 1860

Arg Ser  Ser Pro Val Val Ile  Asp Ala Ser Thr Ala  Ile Asp Ala
1865                 1870                 1875

Pro Ser  Asn Leu Arg Phe Leu  Ala Thr Thr Pro Asn  Ser Leu Leu
1880                 1885                 1890

Val Ser  Trp Gln Pro Pro Arg  Ala Arg Ile Thr Gly  Tyr Ile Ile
1895                 1900                 1905

Lys Tyr  Glu Lys Pro Gly Ser  Pro Pro Arg Glu Val  Val Pro Arg
1910                 1915                 1920

Pro Arg  Pro Gly Val Thr Glu  Ala Thr Ile Thr Gly  Leu Glu Pro
1925                 1930                 1935

Gly Thr  Glu Tyr Thr Ile Tyr  Val Ile Ala Leu Lys  Asn Asn Gln
1940                 1945                 1950

Lys Ser  Glu Pro Leu Ile Gly  Arg Lys Lys Thr Asp  Glu Leu Pro
1955                 1960                 1965

Gln Leu  Val Thr Leu Pro His  Pro Asn Leu His Gly  Pro Glu Ile
1970                 1975                 1980

Leu Asp  Val Pro Ser Thr Val  Gln Lys Thr Pro Phe  Val Thr His
1985                 1990                 1995

Pro Gly  Tyr Asp Thr Gly Asn  Gly Ile Gln Leu Pro  Gly Thr Ser
2000                 2005                 2010
```

Gly Gln Gln Pro Ser Val Gly Gln Gln Met Ile Phe Glu Glu His
2015 2020 2025

Gly Phe Arg Arg Thr Thr Pro Pro Thr Thr Ala Thr Pro Ile Arg
2030 2035 2040

His Arg Pro Arg Pro Tyr Pro Pro Asn Val Gly Gln Glu Ala Leu
2045 2050 2055

Ser Gln Thr Thr Ile Ser Trp Ala Pro Phe Gln Asp Thr Ser Glu
2060 2065 2070

Tyr Ile Ile Ser Cys His Pro Val Gly Thr Asp Glu Glu Pro Leu
2075 2080 2085

Gln Phe Arg Val Pro Gly Thr Ser Thr Ser Ala Thr Leu Thr Gly
2090 2095 2100

Leu Thr Arg Gly Ala Thr Tyr Asn Ile Ile Val Glu Ala Leu Lys
2105 2110 2115

Asp Gln Gln Arg His Lys Val Arg Glu Glu Val Val Thr Val Gly
2120 2125 2130

Asn Ser Val Asn Glu Gly Leu Asn Gln Pro Thr Asp Asp Ser Cys
2135 2140 2145

Phe Asp Pro Tyr Thr Val Ser His Tyr Ala Val Gly Asp Glu Trp
2150 2155 2160

Glu Arg Met Ser Glu Ser Gly Phe Lys Leu Leu Cys Gln Cys Leu
2165 2170 2175

Gly Phe Gly Ser Gly His Phe Arg Cys Asp Ser Ser Arg Trp Cys
2180 2185 2190

His Asp Asn Gly Val Asn Tyr Lys Ile Gly Glu Lys Trp Asp Arg
2195 2200 2205

Gln Gly Glu Asn Gly Gln Met Met Ser Cys Thr Cys Leu Gly Asn
2210 2215 2220

Gly Lys Gly Glu Phe Lys Cys Asp Pro His Glu Ala Thr Cys Tyr
2225 2230 2235

Asp Asp Gly Lys Thr Tyr His Val Gly Glu Gln Trp Gln Lys Glu
2240 2245 2250

Tyr Leu Gly Ala Ile Cys Ser Cys Thr Cys Phe Gly Gly Gln Arg
2255 2260 2265

Gly Trp Arg Cys Asp Asn Cys Arg Arg Pro Gly Gly Glu Pro Ser
2270 2275 2280

Pro Glu Gly Thr Thr Gly Gln Ser Tyr Asn Gln Tyr Ser Gln Arg
2285 2290 2295

Tyr His Gln Arg Thr Asn Thr Asn Val Asn Cys Pro Ile Glu Cys
2300 2305 2310

Phe Met Pro Leu Asp Val Gln Ala Asp Arg Glu Asp Ser Arg Glu
2315 2320 2325

<210> 197
<211> 165
<212> PRT
<213> Homo sapiens

<400> 197

Met Leu Met Pro Lys Lys Asn Arg Ile Ala Ile Tyr Glu Leu Leu Phe
1 5 10 15

Lys Glu Gly Val Met Val Ala Lys Lys Asp Val His Met Pro Lys His
20 25 30

Pro Glu Leu Ala Asp Lys Asn Val Pro Asn Leu His Val Met Lys Ala
35 40 45

Met Gln Ser Leu Lys Ser Arg Gly Tyr Val Lys Glu Gln Phe Ala Trp
50 55 60

Arg His Phe Tyr Trp Tyr Leu Thr Asn Glu Gly Ile Gln Tyr Leu Arg
65 70 75 80

Asp Tyr Leu His Leu Pro Pro Glu Ile Val Pro Ala Thr Leu Arg Arg
85 90 95

Ser Arg Pro Glu Thr Gly Arg Pro Arg Pro Lys Gly Leu Glu Gly Glu
100 105 110

Arg Pro Ala Arg Leu Thr Arg Gly Glu Ala Asp Arg Asp Thr Tyr Arg
115 120 125

Arg Ser Ala Val Pro Pro Gly Ala Asp Lys Lys Ala Glu Ala Gly Ala
130 135 140

Gly Ser Ala Thr Glu Phe Gln Phe Arg Gly Gly Phe Gly Arg Gly Arg
145 150 155 160

Gly Gln Pro Pro Gln
165

<210> 198
<211> 154
<212> PRT
<213> Homo sapiens

<400> 198

Met Ala Thr Lys Ala Val Cys Val Leu Lys Gly Asp Gly Pro Val Gln
1 5 10 15

Gly Ile Ile Asn Phe Glu Gln Lys Glu Ser Asn Gly Pro Val Lys Val
20 25 30

Trp Gly Ser Ile Lys Gly Leu Thr Glu Gly Leu His Gly Phe His Val
35 40 45

His Glu Phe Gly Asp Asn Thr Ala Gly Cys Thr Ser Ala Gly Pro His
50 55 60

```
Phe Asn Pro Leu Ser Arg Lys His Gly Gly Pro Lys Asp Glu Glu Arg
65                  70                  75                  80

His Val Gly Asp Leu Gly Asn Val Thr Ala Asp Lys Asp Gly Val Ala
                85                  90                  95

Asp Val Ser Ile Glu Asp Ser Val Ile Ser Leu Ser Gly Asp His Cys
            100                 105                 110

Ile Ile Gly Arg Thr Leu Val Val His Glu Lys Ala Asp Asp Leu Gly
        115                 120                 125

Lys Gly Gly Asn Glu Glu Ser Thr Lys Thr Gly Asn Ala Gly Ser Arg
    130                 135                 140

Leu Ala Cys Gly Val Ile Gly Ile Ala Gln
145                 150
```

<210> 199
<211> 3256
<212> PRT
<213> Homo sapiens

<400> 199

```
Met Trp Pro Thr Arg Arg Leu Val Thr Ile Lys Arg Ser Gly Val Asp
1               5                   10                  15

Gly Pro His Phe Pro Leu Ser Leu Ser Thr Cys Leu Phe Gly Arg Gly
            20                  25                  30

Ile Glu Cys Asp Ile Arg Ile Gln Leu Pro Val Val Ser Lys Gln His
        35                  40                  45

Cys Lys Ile Glu Ile His Glu Gln Glu Ala Ile Leu His Asn Phe Ser
    50                  55                  60

Ser Thr Asn Pro Thr Gln Val Asn Gly Ser Val Ile Asp Glu Pro Val
65                  70                  75                  80

Arg Leu Lys His Gly Asp Val Ile Thr Ile Ile Asp Arg Ser Phe Arg
                85                  90                  95

Tyr Glu Asn Glu Ser Leu Gln Asn Gly Arg Lys Ser Thr Glu Phe Pro
            100                 105                 110

Arg Lys Ile Arg Glu Gln Glu Pro Ala Arg Arg Val Ser Arg Ser Ser
        115                 120                 125

Phe Ser Ser Asp Pro Asp Glu Lys Ala Gln Asp Ser Lys Ala Tyr Ser
    130                 135                 140

Lys Ile Thr Glu Gly Lys Val Ser Gly Asn Pro Gln Val His Ile Lys
145                 150                 155                 160

Asn Val Lys Glu Asp Ser Thr Ala Asp Asp Ser Lys Asp Ser Val Ala
                165                 170                 175

Gln Gly Thr Thr Asn Val His Ser Ser Glu His Ala Gly Arg Asn Gly
            180                 185                 190
```



```
Arg Asn Ala Ala Asp Pro Ile Ser Gly Asp Phe Lys Glu Ile Ser Ser
        195                 200                 205

Val Lys Leu Val Ser Arg Tyr Gly Glu Leu Lys Ser Val Pro Thr Thr
    210                 215                 220

Gln Cys Leu Asp Asn Ser Lys Lys Asn Glu Ser Pro Phe Trp Lys Leu
225                 230                 235                 240

Tyr Glu Ser Val Lys Lys Glu Leu Asp Val Lys Ser Gln Lys Glu Asn
                245                 250                 255

Val Leu Gln Tyr Cys Arg Lys Ser Gly Leu Gln Thr Asp Tyr Ala Thr
            260                 265                 270

Glu Lys Glu Ser Ala Asp Gly Leu Gln Gly Glu Thr Gln Leu Leu Val
        275                 280                 285

Ser Arg Lys Ser Arg Pro Lys Ser Gly Gly Ser Gly His Ala Val Ala
    290                 295                 300

Glu Pro Ala Ser Pro Glu Gln Glu Leu Asp Gln Asn Lys Gly Lys Gly
305                 310                 315                 320

Arg Asp Val Glu Ser Val Gln Thr Pro Ser Lys Ala Val Gly Ala Ser
                325                 330                 335

Phe Pro Leu Tyr Glu Pro Ala Lys Met Lys Thr Pro Val Gln Tyr Ser
            340                 345                 350

Gln Gln Gln Asn Ser Pro Gln Lys His Lys Asn Lys Asp Leu Tyr Thr
        355                 360                 365

Thr Gly Arg Arg Glu Ser Val Asn Leu Gly Lys Ser Glu Gly Phe Lys
    370                 375                 380

Ala Gly Asp Lys Thr Leu Thr Pro Arg Lys Leu Ser Thr Arg Asn Arg
385                 390                 395                 400

Thr Pro Ala Lys Val Glu Asp Ala Ala Asp Ser Ala Thr Lys Pro Glu
                405                 410                 415

Asn Leu Ser Ser Lys Thr Arg Gly Ser Ile Pro Thr Asp Val Glu Val
            420                 425                 430

Leu Pro Thr Glu Thr Glu Ile His Asn Glu Pro Phe Leu Thr Leu Trp
        435                 440                 445

Leu Thr Gln Val Glu Arg Lys Ile Gln Lys Asp Ser Leu Ser Lys Pro
    450                 455                 460

Glu Lys Leu Gly Thr Thr Ala Gly Gln Met Cys Ser Gly Leu Pro Gly
465                 470                 475                 480

Leu Ser Ser Val Asp Ile Asn Asn Phe Gly Asp Ser Ile Asn Glu Ser
                485                 490                 495

Glu Gly Ile Pro Leu Lys Arg Arg Arg Val Ser Phe Gly Gly His Leu
            500                 505                 510
```

```
Arg Pro Glu Leu Phe Asp Glu Asn Leu Pro Pro Asn Thr Pro Leu Lys
        515                 520                 525

Arg Gly Glu Ala Pro Thr Lys Arg Lys Ser Leu Val Met His Thr Pro
    530                 535                 540

Pro Val Leu Lys Lys Ile Ile Lys Glu Gln Pro Gln Pro Ser Gly Lys
545                 550                 555                 560

Gln Glu Ser Gly Ser Glu Ile His Val Glu Val Lys Ala Gln Ser Leu
                565                 570                 575

Val Ile Ser Pro Pro Ala Pro Ser Pro Arg Lys Thr Pro Val Ala Ser
            580                 585                 590

Asp Gln Arg Arg Arg Ser Cys Lys Thr Ala Pro Ala Ser Ser Ser Lys
        595                 600                 605

Ser Gln Thr Glu Val Pro Lys Arg Gly Gly Glu Arg Val Ala Thr Cys
    610                 615                 620

Leu Gln Lys Arg Val Ser Ile Ser Arg Ser Gln His Asp Ile Leu Gln
625                 630                 635                 640

Met Ile Cys Ser Lys Arg Arg Ser Gly Ala Ser Glu Ala Asn Leu Ile
                645                 650                 655

Val Ala Lys Ser Trp Ala Asp Val Val Lys Leu Gly Ala Lys Gln Thr
            660                 665                 670

Gln Thr Lys Val Ile Lys His Gly Pro Gln Arg Ser Met Asn Lys Arg
        675                 680                 685

Gln Arg Arg Pro Ala Thr Pro Lys Lys Pro Val Gly Glu Val His Ser
    690                 695                 700

Gln Phe Ser Thr Gly His Ala Asn Ser Pro Cys Thr Ile Ile Ile Gly
705                 710                 715                 720

Lys Ala His Thr Glu Lys Val His Val Pro Ala Arg Pro Tyr Arg Val
                725                 730                 735

Leu Asn Asn Phe Ile Ser Asn Gln Lys Met Asp Phe Lys Glu Asp Leu
            740                 745                 750

Ser Gly Ile Ala Glu Met Phe Lys Thr Pro Val Lys Glu Gln Pro Gln
        755                 760                 765

Leu Thr Ser Thr Cys His Ile Ala Ile Ser Asn Ser Glu Asn Leu Leu
    770                 775                 780

Gly Lys Gln Phe Gln Gly Thr Asp Ser Gly Glu Glu Pro Leu Leu Pro
785                 790                 795                 800

Thr Ser Glu Ser Phe Gly Gly Asn Val Phe Phe Ser Ala Gln Asn Ala
                805                 810                 815

Ala Lys Gln Pro Ser Asp Lys Cys Ser Ala Ser Pro Pro Leu Arg Arg
            820                 825                 830
```



```
Gln Cys Ile Arg Glu Asn Gly Asn Val Ala Lys Thr Pro Arg Asn Thr
        835                 840                 845

Tyr Lys Met Thr Ser Leu Glu Thr Lys Thr Ser Asp Thr Glu Thr Glu
    850                 855                 860

Pro Ser Lys Thr Val Ser Thr Val Asn Arg Ser Gly Arg Ser Thr Glu
865                 870                 875                 880

Phe Arg Asn Ile Gln Lys Leu Pro Val Glu Ser Lys Ser Glu Glu Thr
                885                 890                 895

Asn Thr Glu Ile Val Glu Cys Ile Leu Lys Arg Gly Gln Lys Ala Thr
            900                 905                 910

Leu Leu Gln Gln Arg Arg Glu Gly Glu Met Lys Glu Ile Glu Arg Pro
        915                 920                 925

Phe Glu Thr Tyr Lys Glu Asn Ile Glu Leu Lys Glu Asn Asp Glu Lys
    930                 935                 940

Met Lys Ala Met Lys Arg Ser Arg Thr Trp Gly Gln Lys Cys Ala Pro
945                 950                 955                 960

Met Ser Asp Leu Thr Asp Leu Lys Ser Leu Pro Asp Thr Glu Leu Met
                965                 970                 975

Lys Asp Thr Ala Arg Gly Gln Asn Leu Leu Gln Thr Gln Asp His Ala
            980                 985                 990

Lys Ala Pro Lys Ser Glu Lys Gly Lys Ile Thr Lys Met Pro Cys Gln
        995                 1000                1005

Ser Leu Gln Pro Glu Pro Ile Asn Thr Pro Thr His Thr Lys Gln
    1010                1015                1020

Gln Leu Lys Ala Ser Leu Gly Lys Val Gly Val Lys Glu Glu Leu
    1025                1030                1035

Leu Ala Val Gly Lys Phe Thr Arg Thr Ser Gly Glu Thr Thr His
    1040                1045                1050

Thr His Arg Glu Pro Ala Gly Asp Gly Lys Ser Ile Arg Thr Phe
    1055                1060                1065

Lys Glu Ser Pro Lys Gln Ile Leu Asp Pro Ala Ala Arg Val Thr
    1070                1075                1080

Gly Met Lys Lys Trp Pro Arg Thr Pro Lys Glu Glu Ala Gln Ser
    1085                1090                1095

Leu Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Pro Gly
    1100                1105                1110

Pro Ser Glu Glu Ser Met Thr Asp Glu Lys Thr Thr Lys Ile Ala
    1115                1120                1125

Cys Lys Ser Pro Pro Pro Glu Ser Val Asp Thr Pro Thr Ser Thr
```

1130 1135 1140

Lys Gln Trp Pro Lys Arg Ser Leu Arg Lys Ala Asp Val Glu Glu
1145 1150 1155

Glu Phe Leu Ala Leu Arg Lys Leu Thr Pro Ser Ala Gly Lys Ala
1160 1165 1170

Met Leu Thr Pro Lys Pro Ala Gly Gly Asp Glu Lys Asp Ile Lys
1175 1180 1185

Ala Phe Met Gly Thr Pro Val Gln Lys Leu Asp Leu Ala Gly Thr
1190 1195 1200

Leu Pro Gly Ser Lys Arg Gln Leu Gln Thr Pro Lys Glu Lys Ala
1205 1210 1215

Gln Ala Leu Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr
1220 1225 1230

Pro Gly His Thr Glu Glu Leu Val Ala Ala Gly Lys Thr Thr Lys
1235 1240 1245

Ile Pro Cys Asp Ser Pro Gln Ser Asp Pro Val Asp Thr Pro Thr
1250 1255 1260

Ser Thr Lys Gln Arg Pro Lys Arg Ser Ile Arg Lys Ala Asp Val
1265 1270 1275

Glu Gly Glu Leu Leu Ala Cys Arg Asn Leu Met Pro Ser Ala Gly
1280 1285 1290

Lys Ala Met His Thr Pro Lys Pro Ser Val Gly Glu Glu Lys Asp
1295 1300 1305

Ile Ile Ile Phe Val Gly Thr Pro Val Gln Lys Leu Asp Leu Thr
1310 1315 1320

Glu Asn Leu Thr Gly Ser Lys Arg Arg Pro Gln Thr Pro Lys Glu
1325 1330 1335

Glu Ala Gln Ala Leu Glu Asp Leu Thr Gly Phe Lys Glu Leu Phe
1340 1345 1350

Gln Thr Pro Gly His Thr Glu Glu Ala Val Ala Ala Gly Lys Thr
1355 1360 1365

Thr Lys Met Pro Cys Glu Ser Ser Pro Pro Glu Ser Ala Asp Thr
1370 1375 1380

Pro Thr Ser Thr Arg Arg Gln Pro Lys Thr Pro Leu Glu Lys Arg
1385 1390 1395

Asp Val Gln Lys Glu Leu Ser Ala Leu Lys Lys Leu Thr Gln Thr
1400 1405 1410

Ser Gly Glu Thr Thr His Thr Asp Lys Val Pro Gly Gly Glu Asp
1415 1420 1425

Lys Ser Ile Asn Ala Phe Arg Glu Thr Ala Lys Gln Lys Leu Asp
1430 1435 1440

Pro Ala Ala Ser Val Thr Gly Ser Lys Arg His Pro Lys Thr Lys
1445 1450 1455

Glu Lys Ala Gln Pro Leu Glu Asp Leu Ala Gly Trp Lys Glu Leu
1460 1465 1470

Phe Gln Thr Pro Val Cys Thr Asp Lys Pro Thr Thr His Glu Lys
1475 1480 1485

Thr Thr Lys Ile Ala Cys Arg Ser Gln Pro Asp Pro Val Asp Thr
1490 1495 1500

Pro Thr Ser Ser Lys Pro Gln Ser Lys Arg Ser Leu Arg Lys Val
1505 1510 1515

Asp Val Glu Glu Glu Phe Phe Ala Leu Arg Lys Arg Thr Pro Ser
1520 1525 1530

Ala Gly Lys Ala Met His Thr Pro Lys Pro Ala Val Ser Gly Glu
1535 1540 1545

Lys Asn Ile Tyr Ala Phe Met Gly Thr Pro Val Gln Lys Leu Asp
1550 1555 1560

Leu Thr Glu Asn Leu Thr Gly Ser Lys Arg Arg Leu Gln Thr Pro
1565 1570 1575

Lys Glu Lys Ala Gln Ala Leu Glu Asp Leu Ala Gly Phe Lys Glu
1580 1585 1590

Leu Phe Gln Thr Arg Gly His Thr Glu Glu Ser Met Thr Asn Asp
1595 1600 1605

Lys Thr Ala Lys Val Ala Cys Lys Ser Ser Gln Pro Asp Leu Asp
1610 1615 1620

Lys Asn Pro Ala Ser Ser Lys Arg Arg Leu Lys Thr Ser Leu Gly
1625 1630 1635

Lys Val Gly Val Lys Glu Glu Leu Leu Ala Val Gly Lys Leu Thr
1640 1645 1650

Gln Thr Ser Gly Glu Thr Thr His Thr His Thr Glu Pro Thr Gly
1655 1660 1665

Asp Gly Lys Ser Met Lys Ala Phe Met Glu Ser Pro Lys Gln Ile
1670 1675 1680

Leu Asp Ser Ala Ala Ser Leu Thr Gly Ser Lys Arg Gln Leu Arg
1685 1690 1695

Thr Pro Lys Gly Lys Ser Glu Val Pro Glu Asp Leu Ala Gly Phe
1700 1705 1710

Ile Glu Leu Phe Gln Thr Pro Ser His Thr Lys Glu Ser Met Thr
1715 1720 1725

Asn Glu Lys Thr Thr Lys Val Ser Tyr Arg Ala Ser Gln Pro Asp
1730 1735 1740

Leu Val Asp Thr Pro Thr Ser Ser Lys Pro Gln Pro Lys Arg Ser
1745 1750 1755

Leu Arg Lys Ala Asp Thr Glu Glu Glu Phe Leu Ala Phe Arg Lys
1760 1765 1770

Gln Thr Pro Ser Ala Gly Lys Ala Met His Thr Pro Lys Pro Ala
1775 1780 1785

Val Gly Glu Glu Lys Asp Ile Asn Thr Phe Leu Gly Thr Pro Val
1790 1795 1800

Gln Lys Leu Asp Gln Pro Gly Asn Leu Pro Gly Ser Asn Arg Arg
1805 1810 1815

Leu Gln Thr Arg Lys Glu Lys Ala Gln Ala Leu Glu Glu Leu Thr
1820 1825 1830

Gly Phe Arg Glu Leu Phe Gln Thr Pro Cys Thr Asp Asn Pro Thr
1835 1840 1845

Ala Asp Glu Lys Thr Thr Lys Lys Ile Leu Cys Lys Ser Pro Gln
1850 1855 1860

Ser Asp Pro Ala Asp Thr Pro Thr Asn Thr Lys Gln Arg Pro Lys
1865 1870 1875

Arg Ser Leu Lys Lys Ala Asp Val Glu Glu Glu Phe Leu Ala Phe
1880 1885 1890

Arg Lys Leu Thr Pro Ser Ala Gly Lys Ala Met His Thr Pro Lys
1895 1900 1905

Ala Ala Val Gly Glu Glu Lys Asp Ile Asn Thr Phe Val Gly Thr
1910 1915 1920

Pro Val Glu Lys Leu Asp Leu Leu Gly Asn Leu Pro Gly Ser Lys
1925 1930 1935

Arg Arg Pro Gln Thr Pro Lys Glu Lys Ala Lys Ala Leu Glu Asp
1940 1945 1950

Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Pro Gly His Thr Glu
1955 1960 1965

Glu Ser Met Thr Asp Asp Lys Ile Thr Glu Val Ser Cys Lys Ser
1970 1975 1980

Pro Gln Pro Asp Pro Val Lys Thr Pro Thr Ser Ser Lys Gln Arg
1985 1990 1995

Leu Lys Ile Ser Leu Gly Lys Val Gly Val Lys Glu Glu Val Leu
2000 2005 2010

Pro Val Gly Lys Leu Thr Gln Thr Ser Gly Lys Thr Thr Gln Thr
2015 2020 2025

His Arg Glu Thr Ala Gly Asp Gly Lys Ser Ile Lys Ala Phe Lys
2030 2035 2040

Glu Ser Ala Lys Gln Met Leu Asp Pro Ala Asn Tyr Gly Thr Gly
2045 2050 2055

Met Glu Arg Trp Pro Arg Thr Pro Lys Glu Glu Ala Gln Ser Leu
2060 2065 2070

Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Pro Asp His
2075 2080 2085

Thr Glu Glu Ser Thr Thr Asp Asp Lys Thr Thr Lys Ile Ala Cys
2090 2095 2100

Lys Ser Pro Pro Pro Glu Ser Met Asp Thr Pro Thr Ser Thr Arg
2105 2110 2115

Arg Arg Pro Lys Thr Pro Leu Gly Lys Arg Asp Ile Val Glu Glu
2120 2125 2130

Leu Ser Ala Leu Lys Gln Leu Thr Gln Thr Thr His Thr Asp Lys
2135 2140 2145

Val Pro Gly Asp Glu Asp Lys Gly Ile Asn Val Phe Arg Glu Thr
2150 2155 2160

Ala Lys Gln Lys Leu Asp Pro Ala Ala Ser Val Thr Gly Ser Lys
2165 2170 2175

Arg Gln Pro Arg Thr Pro Lys Gly Lys Ala Gln Pro Leu Glu Asp
2180 2185 2190

Leu Ala Gly Leu Lys Glu Leu Phe Gln Thr Pro Val Cys Thr Asp
2195 2200 2205

Lys Pro Thr Thr His Glu Lys Thr Thr Lys Ile Ala Cys Arg Ser
2210 2215 2220

Pro Gln Pro Asp Pro Val Gly Thr Pro Thr Ile Phe Lys Pro Gln
2225 2230 2235

Ser Lys Arg Ser Leu Arg Lys Ala Asp Val Glu Glu Glu Ser Leu
2240 2245 2250

Ala Leu Arg Lys Arg Thr Pro Ser Val Gly Lys Ala Met Asp Thr
2255 2260 2265

Pro Lys Pro Ala Gly Gly Asp Glu Lys Asp Met Lys Ala Phe Met
2270 2275 2280

Gly Thr Pro Val Gln Lys Leu Asp Leu Pro Gly Asn Leu Pro Gly
2285 2290 2295

Ser Lys Arg Trp Pro Gln Thr Pro Lys Glu Lys Ala Gln Ala Leu
2300 2305 2310

Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Pro Gly Thr

2315 2320 2325

Asp Lys Pro Thr Thr Asp Glu Lys Thr Thr Lys Ile Ala Cys Lys
2330 2335 2340

Ser Pro Gln Pro Asp Pro Val Asp Thr Pro Ala Ser Thr Lys Gln
2345 2350 2355

Arg Pro Lys Arg Asn Leu Arg Lys Ala Asp Val Glu Glu Glu Phe
2360 2365 2370

Leu Ala Leu Arg Lys Arg Thr Pro Ser Ala Gly Lys Ala Met Asp
2375 2380 2385

Thr Pro Lys Pro Ala Val Ser Asp Glu Lys Asn Ile Asn Thr Phe
2390 2395 2400

Val Glu Thr Pro Val Gln Lys Leu Asp Leu Leu Gly Asn Leu Pro
2405 2410 2415

Gly Ser Lys Arg Gln Pro Gln Thr Pro Lys Glu Lys Ala Glu Ala
2420 2425 2430

Leu Glu Asp Leu Val Gly Phe Lys Glu Leu Phe Gln Thr Pro Gly
2435 2440 2445

His Thr Glu Glu Ser Met Thr Asp Asp Lys Ile Thr Glu Val Ser
2450 2455 2460

Cys Lys Ser Pro Gln Pro Glu Ser Phe Lys Thr Ser Arg Ser Ser
2465 2470 2475

Lys Gln Arg Leu Lys Ile Pro Leu Val Lys Val Asp Met Lys Glu
2480 2485 2490

Glu Pro Leu Ala Val Ser Lys Leu Thr Arg Thr Ser Gly Glu Thr
2495 2500 2505

Thr Gln Thr His Thr Glu Pro Thr Gly Asp Ser Lys Ser Ile Lys
2510 2515 2520

Ala Phe Lys Glu Ser Pro Lys Gln Ile Leu Asp Pro Ala Ala Ser
2525 2530 2535

Val Thr Gly Ser Arg Arg Gln Leu Arg Thr Arg Lys Glu Lys Ala
2540 2545 2550

Arg Ala Leu Glu Asp Leu Val Asp Phe Lys Glu Leu Phe Ser Ala
2555 2560 2565

Pro Gly His Thr Glu Glu Ser Met Thr Ile Asp Lys Asn Thr Lys
2570 2575 2580

Ile Pro Cys Lys Ser Pro Pro Pro Glu Leu Thr Asp Thr Ala Thr
2585 2590 2595

Ser Thr Lys Arg Cys Pro Lys Thr Arg Pro Arg Lys Glu Val Lys
2600 2605 2610

Glu Glu Leu Ser Ala Val Glu Arg Leu Thr Gln Thr Ser Gly Gln
2615 2620 2625

Ser Thr His Thr His Lys Glu Pro Ala Ser Gly Asp Glu Gly Ile
2630 2635 2640

Lys Val Leu Lys Gln Arg Ala Lys Lys Lys Pro Asn Pro Val Glu
2645 2650 2655

Glu Glu Pro Ser Arg Arg Arg Pro Arg Ala Pro Lys Glu Lys Ala
2660 2665 2670

Gln Pro Leu Glu Asp Leu Ala Gly Phe Thr Glu Leu Ser Glu Thr
2675 2680 2685

Ser Gly His Thr Gln Glu Ser Leu Thr Ala Gly Lys Ala Thr Lys
2690 2695 2700

Ile Pro Cys Glu Ser Pro Pro Leu Glu Val Val Asp Thr Thr Ala
2705 2710 2715

Ser Thr Lys Arg His Leu Arg Thr Arg Val Gln Lys Val Gln Val
2720 2725 2730

Lys Glu Glu Pro Ser Ala Val Lys Phe Thr Gln Thr Ser Gly Glu
2735 2740 2745

Thr Thr Asp Ala Asp Lys Glu Pro Ala Gly Glu Asp Lys Gly Ile
2750 2755 2760

Lys Ala Leu Lys Glu Ser Ala Lys Gln Thr Pro Ala Pro Ala Ala
2765 2770 2775

Ser Val Thr Gly Ser Arg Arg Arg Pro Arg Ala Pro Arg Glu Ser
2780 2785 2790

Ala Gln Ala Ile Glu Asp Leu Ala Gly Phe Lys Asp Pro Ala Ala
2795 2800 2805

Gly His Thr Glu Glu Ser Met Thr Asp Asp Lys Thr Thr Lys Ile
2810 2815 2020

Pro Cys Lys Ser Ser Pro Glu Leu Glu Asp Thr Ala Thr Ser Ser
2825 2830 2835

Lys Arg Arg Pro Arg Thr Arg Ala Gln Lys Val Glu Val Lys Glu
2840 2845 2850

Glu Leu Leu Ala Val Gly Lys Leu Thr Gln Thr Ser Gly Glu Thr
2855 2860 2865

Thr His Thr Asp Lys Glu Pro Val Gly Glu Gly Lys Gly Thr Lys
2870 2875 2880

Ala Phe Lys Gln Pro Ala Lys Arg Asn Val Asp Ala Glu Asp Val
2885 2890 2895

Ile Gly Ser Arg Arg Gln Pro Arg Ala Pro Lys Glu Lys Ala Gln
2900 2905 2910

Pro Leu Glu Asp Leu Ala Ser Phe Gln Glu Leu Ser Gln Thr Pro
2915 2920 2925

Gly His Thr Glu Glu Leu Ala Asn Gly Ala Ala Asp Ser Phe Thr
2930 2935 2940

Ser Ala Pro Lys Gln Thr Pro Asp Ser Gly Lys Pro Leu Lys Ile
2945 2950 2955

Ser Arg Arg Val Leu Arg Ala Pro Lys Val Glu Pro Val Gly Asp
2960 2965 2970

Val Val Ser Thr Arg Asp Pro Val Lys Ser Gln Ser Lys Ser Asn
2975 2980 2985

Thr Ser Leu Pro Pro Leu Pro Phe Lys Arg Gly Gly Gly Lys Asp
2990 2995 3000

Gly Ser Val Thr Gly Thr Lys Arg Leu Arg Cys Met Pro Ala Pro
3005 3010 3015

Glu Glu Ile Val Glu Glu Leu Pro Ala Ser Lys Lys Gln Arg Val
3020 3025 3030

Ala Pro Arg Ala Arg Gly Lys Ser Ser Glu Pro Val Val Ile Met
3035 3040 3045

Lys Arg Ser Leu Arg Thr Ser Ala Lys Arg Ile Glu Pro Ala Glu
3050 3055 3060

Glu Leu Asn Ser Asn Asp Met Lys Thr Asn Lys Glu Glu His Lys
3065 3070 3075

Leu Gln Asp Ser Val Pro Glu Asn Lys Gly Ile Ser Leu Arg Ser
3080 3085 3090

Arg Arg Gln Asp Lys Thr Glu Ala Glu Gln Gln Ile Thr Glu Val
3095 3100 3105

Phe Val Leu Ala Glu Arg Ile Glu Ile Asn Arg Asn Glu Lys Lys
3110 3115 3120

Pro Met Lys Thr Ser Pro Glu Met Asp Ile Gln Asn Pro Asp Asp
3125 3130 3135

Gly Ala Arg Lys Pro Ile Pro Arg Asp Lys Val Thr Glu Asn Lys
3140 3145 3150

Arg Cys Leu Arg Ser Ala Arg Gln Asn Glu Ser Ser Gln Pro Lys
3155 3160 3165

Val Ala Glu Glu Ser Gly Gly Gln Lys Ser Ala Lys Val Leu Met
3170 3175 3180

Gln Asn Gln Lys Gly Lys Gly Glu Ala Gly Asn Ser Asp Ser Met
3185 3190 3195

Cys Leu Arg Ser Arg Lys Thr Lys Ser Gln Pro Ala Ala Ser Thr
3200 3205 3210

Leu Glu Ser Lys Ser Val Gln Arg Val Thr Arg Ser Val Lys Arg
3215 3220 3225

Cys Ala Glu Asn Pro Lys Lys Ala Glu Asp Asn Val Cys Val Lys
3230 3235 3240

Lys Ile Thr Thr Arg Ser His Arg Asp Ser Glu Asp Ile
3245 3250 3255

<210> 200
<211> 478
<212> PRT
<213> Homo sapiens

<400> 200

Met Ala Gly Val Glu Glu Val Ala Ala Ser Gly Ser His Leu Asn Gly
1 5 10 15

Asp Leu Asp Pro Asp Asp Arg Glu Glu Gly Ala Ala Ser Thr Ala Glu
20 25 30

Glu Ala Ala Lys Lys Lys Arg Arg Lys Lys Lys Lys Ser Lys Gly Pro
35 40 45

Ser Ala Ala Gly Glu Gln Glu Pro Asp Lys Glu Ser Gly Ala Ser Val
50 55 60

Asp Glu Val Ala Arg Gln Leu Glu Arg Ser Ala Leu Glu Asp Lys Glu
65 70 75 80

Arg Asp Glu Asp Asp Glu Asp Gly Asp Gly Asp Gly Asp Gly Ala Thr
85 90 95

Gly Lys Lys Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Lys Val Gln
100 105 110

Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val
115 120 125

Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg
130 135 140

Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln
145 150 155 160

Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His
165 170 175

Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr
180 185 190

Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile
195 200 205

Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Phe Pro Thr Gly Cys Ser
210 215 220

Leu Asn Asn Cys Ala Ala His Tyr Thr Pro Asn Ala Gly Asp Thr Thr
225 230 235 240

Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Asp Phe Gly Thr His Ile
245 250 255

Ser Gly Arg Ile Ile Asp Cys Ala Phe Thr Val Thr Phe Asn Pro Lys
260 265 270

Tyr Asp Thr Leu Leu Lys Ala Val Lys Asp Ala Thr Asn Thr Gly Ile
275 280 285

Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile
290 295 300

Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr
305 310 315 320

Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Gln Tyr
325 330 335

Arg Ile His Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala
340 345 350

Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Glu Thr Phe Gly Ser
355 360 365

Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met
370 375 380

Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys
385 390 395 400

His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
405 410 415

Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu
420 425 430

Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Tyr Pro Pro Leu Cys
435 440 445

Asp Ile Lys Gly Ser Tyr Thr Ala Gln Phe Glu His Thr Ile Leu Leu
450 455 460

Arg Pro Thr Cys Lys Glu Val Val Ser Arg Gly Asp Asp Tyr
465 470 475

<210> 201
<211> 488
<212> PRT
<213> Homo sapiens

<400> 201

Met His Gly Arg Lys Asp Asp Ala Gln Lys Gln Pro Val Lys Asn Gln
1 5 10 15

Leu Gly Leu Asn Pro Gln Ser His Leu Pro Glu Leu Gln Leu Phe Gln
20 25 30

Ala Glu Gly Lys Ile Tyr Lys Tyr Asp His Met Glu Lys Ser Val Asn
35 40 45

Ser Ser Ser Leu Val Ser Pro Pro Gln Arg Ile Ser Ser Thr Val Lys
50 55 60

Thr His Ile Ser His Ile Tyr Glu Cys Asn Phe Val Asp Ser Leu Phe
65 70 75 80

Thr Gln Lys Glu Lys Ala Asn Ile Gly Thr Glu His Tyr Lys Cys Asn
85 90 95

Glu Arg Gly Lys Ala Phe His Gln Gly Leu His Phe Thr Ile His Gln
100 105 110

Ile Ile His Thr Lys Glu Thr Gln Phe Lys Cys Asp Ile Cys Gly Lys
115 120 125

Ile Phe Asn Lys Lys Ser Asn Leu Ala Ser His Gln Arg Ile His Thr
130 135 140

Gly Glu Lys Pro Tyr Lys Cys Asn Glu Cys Gly Lys Val Phe His Asn
145 150 155 160

Met Ser His Leu Ala Gln His Arg Arg Ile His Thr Gly Glu Lys Pro
165 170 175

Tyr Lys Cys Asn Glu Cys Gly Lys Val Phe Asn Gln Ile Ser His Leu
180 185 190

Ala Gln His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Lys Cys Asn
195 200 205

Glu Cys Gly Lys Val Phe His Gln Ile Ser His Leu Ala Gln His Arg
210 215 220

Thr Ile His Thr Gly Glu Lys Pro Tyr Glu Cys Asn Lys Cys Gly Lys
225 230 235 240

Val Phe Ser Arg Asn Ser Tyr Leu Val Gln His Leu Ile Ile His Thr
245 250 255

Gly Glu Lys Pro Tyr Arg Cys Asn Val Cys Gly Lys Val Phe Ser His
260 265 270

Lys Ser Ser Leu Val Asn His Trp Arg Ile His Thr Gly Glu Lys Pro
275 280 285

Tyr Lys Cys Asn Glu Cys Gly Lys Val Phe Ser His Lys Ser Ser Leu
290 295 300

Val Asn His Trp Arg Ile His Thr Gly Glu Lys Pro Tyr Lys Cys Asn
305 310 315 320

Glu Cys Gly Lys Val Phe Ser Arg Asn Ser Tyr Leu Ala Gln His Leu
325 330 335

Ile Ile His Ala Gly Glu Lys Pro Tyr Lys Cys Asp Glu Cys Asp Lys
340 345 350

Ala Phe Ser Gln Asn Ser His Leu Val Gln His His Arg Ile His Thr

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        355                 360                 365

Gly Glu Lys Pro Tyr Lys Cys Asp Glu Cys Gly Lys Val Phe Ser Gln
    370                 375                 380

Asn Ser Tyr Leu Ala Tyr His Trp Arg Ile His Thr Gly Glu Lys Ala
385                 390                 395                 400

Tyr Lys Cys Asn Glu Cys Gly Lys Val Phe Gly Leu Asn Ser Ser Leu
                405                 410                 415

Ala His His Arg Lys Ile His Thr Gly Glu Lys Pro Phe Lys Cys Asn
            420                 425                 430

Glu Cys Gly Lys Ala Phe Ser Met Arg Ser Ser Leu Thr Asn His His
        435                 440                 445

Ala Ile His Thr Gly Glu Lys His Phe Lys Cys Asn Glu Cys Gly Lys
    450                 455                 460

Leu Phe Arg Asp Asn Ser Tyr Leu Val Arg His Gln Arg Phe His Ala
465                 470                 475                 480

Gly Lys Lys Ser Asn Thr Cys Asn
                485

<210>  202
<211>  553
<212>  PRT
<213>  Homo sapiens

<400>  202

Met Leu Ser Val Arg Val Ala Ala Ala Val Val Arg Ala Leu Pro Arg
1               5                   10                  15

Arg Ala Gly Leu Val Ser Arg Asn Ala Leu Gly Ser Ser Phe Ile Ala
            20                  25                  30

Ala Arg Asn Phe His Ala Ser Asn Thr His Leu Gln Lys Thr Gly Thr
        35                  40                  45

Ala Glu Met Ser Ser Ile Leu Glu Glu Arg Ile Leu Gly Ala Asp Thr
    50                  55                  60

Ser Val Asp Leu Glu Glu Thr Gly Arg Val Leu Ser Ile Gly Asp Gly
65                  70                  75                  80

Ile Ala Arg Val His Gly Leu Arg Asn Val Gln Ala Glu Glu Met Val
                85                  90                  95

Glu Phe Ser Ser Gly Leu Lys Gly Met Ser Leu Asn Leu Glu Pro Asp
            100                 105                 110

Asn Val Gly Val Val Val Phe Gly Asn Asp Lys Leu Ile Lys Glu Gly
        115                 120                 125

Asp Ile Val Lys Arg Thr Gly Ala Ile Val Asp Val Pro Val Gly Glu
    130                 135                 140

Glu Leu Leu Gly Arg Val Val Asp Ala Leu Gly Asn Ala Ile Asp Gly
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145                 150                 155                 160

Lys Gly Pro Ile Gly Ser Lys Thr Arg Arg Arg Val Gly Leu Lys Ala
                165                 170                 175

Pro Gly Ile Ile Pro Arg Ile Ser Val Arg Glu Pro Met Gln Thr Gly
            180                 185                 190

Ile Lys Ala Val Asp Ser Leu Val Pro Ile Gly Arg Gly Gln Arg Glu
        195                 200                 205

Leu Ile Ile Gly Asp Arg Gln Thr Gly Lys Thr Ser Ile Ala Ile Asp
    210                 215                 220

Thr Ile Ile Asn Gln Lys Arg Phe Asn Asp Gly Ser Asp Glu Lys Lys
225                 230                 235                 240

Lys Leu Tyr Cys Ile Tyr Val Ala Ile Gly Gln Lys Arg Ser Thr Val
                245                 250                 255

Ala Gln Leu Val Lys Arg Leu Thr Asp Ala Asp Ala Met Lys Tyr Thr
            260                 265                 270

Ile Val Val Ser Ala Thr Ala Ser Asp Ala Ala Pro Leu Gln Tyr Leu
        275                 280                 285

Ala Pro Tyr Ser Gly Cys Ser Met Gly Glu Tyr Phe Arg Asp Asn Gly
    290                 295                 300

Lys His Ala Leu Ile Ile Tyr Asp Asp Leu Ser Lys Gln Ala Val Ala
305                 310                 315                 320

Tyr Arg Gln Met Ser Leu Leu Leu Arg Arg Pro Pro Gly Arg Glu Ala
                325                 330                 335

Tyr Pro Gly Asp Val Phe Tyr Leu His Ser Arg Leu Leu Glu Arg Ala
            340                 345                 350

Ala Lys Met Asn Asp Ala Phe Gly Gly Gly Ser Leu Thr Ala Leu Pro
        355                 360                 365

Val Ile Glu Thr Gln Ala Gly Asp Val Ser Ala Tyr Ile Pro Thr Asn
    370                 375                 380

Val Ile Ser Ile Thr Asp Gly Gln Ile Phe Leu Glu Thr Glu Leu Phe
385                 390                 395                 400

Tyr Lys Gly Ile Arg Pro Ala Ile Asn Val Gly Leu Ser Val Ser Arg
                405                 410                 415

Val Gly Ser Ala Ala Gln Thr Arg Ala Met Lys Gln Val Ala Gly Thr
            420                 425                 430

Met Lys Leu Glu Leu Ala Gln Tyr Arg Glu Val Ala Ala Phe Ala Gln
        435                 440                 445

Phe Gly Ser Asp Leu Asp Ala Ala Thr Gln Gln Leu Leu Ser Arg Gly
    450                 455                 460
```

Val Arg Leu Thr Glu Leu Leu Lys Gln Gly Gln Tyr Ser Pro Met Ala
465 470 475 480

Ile Glu Glu Gln Val Ala Val Ile Tyr Ala Gly Val Arg Gly Tyr Leu
485 490 495

Asp Lys Leu Glu Pro Ser Lys Ile Thr Lys Phe Glu Asn Ala Phe Leu
500 505 510

Ser His Val Val Ser Gln His Gln Ala Leu Leu Gly Thr Ile Arg Ala
515 520 525

Asp Gly Lys Ile Ser Glu Gln Ser Asp Ala Lys Leu Lys Glu Ile Val
530 535 540

Thr Asn Phe Leu Ala Gly Phe Glu Ala
545 550

<210> 203
<211> 462
<212> PRT
<213> Homo sapiens

<400> 203

Met Gly Lys Glu Lys Thr His Ile Asn Ile Val Val Ile Gly His Val
1 5 10 15

Asp Ser Gly Lys Ser Thr Thr Thr Gly His Leu Ile Tyr Lys Cys Gly
20 25 30

Gly Ile Asp Lys Arg Thr Ile Glu Lys Phe Glu Lys Glu Ala Ala Glu
35 40 45

Met Gly Lys Gly Ser Phe Lys Tyr Ala Trp Val Leu Asp Lys Leu Lys
50 55 60

Ala Glu Arg Glu Arg Gly Ile Thr Ile Asp Ile Ser Leu Trp Lys Phe
65 70 75 80

Glu Thr Ser Lys Tyr Tyr Val Thr Ile Ile Asp Ala Pro Gly His Arg
85 90 95

Asp Phe Ile Lys Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala
100 105 110

Val Leu Ile Val Ala Ala Gly Val Gly Glu Phe Glu Ala Gly Ile Ser
115 120 125

Lys Asn Gly Gln Thr Arg Glu His Ala Leu Leu Ala Tyr Thr Leu Gly
130 135 140

Val Lys Gln Leu Ile Val Gly Val Asn Lys Met Asp Ser Thr Glu Pro
145 150 155 160

Pro Tyr Ser Gln Lys Arg Tyr Glu Glu Ile Val Lys Glu Val Ser Thr
165 170 175

Tyr Ile Lys Lys Ile Gly Tyr Asn Pro Asp Thr Val Ala Phe Val Pro
180 185 190

Ile Ser Gly Trp Asn Gly Asp Asn Met Leu Glu Pro Ser Ala Asn Met
195 200 205

Pro Trp Phe Lys Gly Trp Lys Val Thr Arg Lys Asp Gly Asn Ala Ser
210 215 220

Gly Thr Thr Leu Leu Glu Ala Val Asp Cys Ile Leu Pro Pro Thr Arg
225 230 235 240

Pro Thr Asp Lys Pro Leu Arg Leu Pro Leu Gln Asp Val Tyr Lys Ile
245 250 255

Gly Gly Ile Gly Thr Val Pro Val Gly Arg Val Glu Thr Gly Val Leu
260 265 270

Lys Pro Gly Met Val Val Thr Phe Ala Pro Val Asn Val Thr Thr Glu
275 280 285

Val Lys Ser Val Glu Met His His Glu Ala Leu Ser Glu Ala Leu Pro
290 295 300

Gly Asp Asn Val Gly Phe Asn Val Lys Asn Val Ser Val Lys Asp Val
305 310 315 320

Arg Arg Gly Asn Val Ala Gly Asp Ser Lys Asn Asp Pro Pro Met Glu
325 330 335

Ala Ala Gly Phe Thr Ala Gln Val Ile Ile Leu Asn His Pro Gly Gln
340 345 350

Ile Ser Ala Gly Tyr Ala Pro Val Leu Asp Cys His Thr Ala His Ile
355 360 365

Ala Cys Lys Phe Ala Glu Leu Lys Glu Lys Ile Asp Arg Arg Ser Gly
370 375 380

Lys Lys Leu Glu Asp Gly Pro Lys Phe Leu Lys Ser Gly Asp Ala Ala
385 390 395 400

Ile Val Asp Met Val Pro Gly Lys Pro Met Cys Val Glu Ser Phe Ser
405 410 415

Asp Tyr Pro Pro Leu Gly Arg Phe Ala Val Arg Asp Met Arg Gln Thr
420 425 430

Val Ala Val Gly Val Ile Lys Ala Val Asp Lys Lys Ala Ala Gly Ala
435 440 445

Gly Lys Val Thr Lys Ser Ala Gln Lys Ala Gln Lys Ala Lys
450 455 460

<210> 204
<211> 1069
<212> PRT
<213> Homo sapiens

<400> 204

Met Leu Arg Met Arg Thr Ala Gly Trp Ala Arg Gly Trp Cys Leu Gly
1 5 10 15

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Cys Cys Leu Leu Leu Pro Leu Ser Phe Ser Leu Ala Ala Ala Lys Gln
            20                  25                  30

Leu Leu Arg Tyr Arg Leu Ala Glu Glu Gly Pro Ala Asp Val Arg Ile
        35                  40                  45

Gly Asn Val Ala Ser Asp Leu Gly Ile Val Thr Gly Ser Gly Glu Val
    50                  55                  60

Thr Phe Ser Leu Glu Ser Gly Ser Glu Tyr Leu Lys Ile Asp Asn Leu
65                  70                  75                  80

Thr Gly Glu Leu Ser Thr Ser Glu Arg Arg Ile Asp Arg Glu Lys Leu
                85                  90                  95

Pro Gln Cys Gln Met Ile Phe Asp Glu Asn Glu Cys Phe Leu Asp Phe
            100                 105                 110

Glu Val Ser Val Ile Gly Pro Ser Gln Ser Trp Val Asp Leu Phe Glu
        115                 120                 125

Gly Gln Val Ile Val Leu Asp Ile Asn Asp Asn Thr Pro Thr Phe Pro
    130                 135                 140

Ser Pro Val Leu Thr Leu Thr Val Glu Glu Asn Arg Pro Val Gly Thr
145                 150                 155                 160

Leu Tyr Leu Leu Pro Thr Ala Thr Asp Arg Asp Phe Gly Arg Asn Gly
                165                 170                 175

Ile Glu Arg Tyr Glu Leu Leu Gln Glu Pro Gly Gly Gly Gly Ser Gly
            180                 185                 190

Gly Glu Ser Arg Arg Ala Gly Ala Ala Asp Ser Ala Pro Tyr Pro Gly
        195                 200                 205

Gly Gly Gly Asn Gly Ala Ser Gly Gly Gly Ser Gly Gly Ser Lys Arg
    210                 215                 220

Arg Leu Asp Ala Ser Glu Gly Gly Gly Gly Thr Asn Pro Gly Gly Arg
225                 230                 235                 240

Ser Ser Val Phe Glu Leu Gln Val Ala Asp Thr Pro Asp Gly Glu Lys
                245                 250                 255

Gln Pro Gln Leu Ile Val Lys Gly Ala Leu Asp Arg Glu Gln Arg Asp
            260                 265                 270

Ser Tyr Glu Leu Thr Leu Arg Val Arg Asp Gly Gly Asp Pro Pro Arg
        275                 280                 285

Ser Ser Gln Ala Ile Leu Arg Val Leu Ile Thr Asp Val Asn Asp Asn
    290                 295                 300

Ser Pro Arg Phe Glu Lys Ser Val Tyr Glu Ala Asp Leu Ala Glu Asn
305                 310                 315                 320

Ser Ala Pro Gly Thr Pro Ile Leu Gln Leu Arg Ala Ala Asp Leu Asp
                325                 330                 335
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Val Gly Val Asn Gly Gln Ile Glu Tyr Val Phe Gly Ala Ala Thr Glu
            340                 345                 350

Ser Val Arg Arg Leu Leu Arg Leu Asp Glu Thr Ser Gly Trp Leu Ser
        355                 360                 365

Val Leu His Arg Ile Asp Arg Glu Glu Val Asn Gln Leu Arg Phe Thr
    370                 375                 380

Val Met Ala Arg Asp Arg Gly Gln Pro Pro Lys Thr Asp Lys Ala Thr
385                 390                 395                 400

Val Val Leu Asn Ile Lys Asp Glu Asn Asp Asn Val Pro Ser Ile Glu
                405                 410                 415

Ile Arg Lys Ile Gly Arg Ile Pro Leu Lys Asp Gly Val Ala Asn Val
            420                 425                 430

Ala Glu Asp Val Leu Val Asp Thr Pro Ile Ala Leu Val Gln Val Ser
        435                 440                 445

Asp Arg Asp Gln Gly Glu Asn Gly Val Val Thr Cys Thr Val Val Gly
    450                 455                 460

Asp Val Pro Phe Gln Leu Lys Pro Ala Ser Asp Thr Glu Gly Asp Gln
465                 470                 475                 480

Asn Lys Lys Lys Tyr Phe Leu His Thr Ser Thr Pro Leu Asp Tyr Glu
                485                 490                 495

Ala Thr Arg Glu Phe Asn Val Val Ile Val Ala Val Asp Ser Gly Ser
            500                 505                 510

Pro Ser Leu Ser Ser Lys Asn Ser Leu Ile Val Lys Val Gly Asp Thr
        515                 520                 525

Asn Asp Asn Pro Pro Met Phe Gly Gln Ser Val Val Glu Val Tyr Phe
    530                 535                 540

Pro Glu Asn Asn Ile Pro Gly Glu Arg Val Ala Thr Val Leu Ala Thr
545                 550                 555                 560

Asp Ala Asp Ser Gly Lys Asn Ala Glu Ile Ala Tyr Ser Leu Asp Ser
                565                 570                 575

Ser Val Met Gly Ile Phe Ala Ile Asp Pro Asp Ser Gly Asp Ile Leu
            580                 585                 590

Val Asn Thr Val Leu Asp Arg Glu Gln Thr Asp Arg Tyr Glu Phe Lys
        595                 600                 605

Val Asn Ala Lys Asp Lys Gly Ile Pro Val Leu Gln Gly Ser Thr Thr
    610                 615                 620

Val Ile Val Gln Val Ala Asp Lys Asn Asp Asn Asp Pro Lys Phe Met
625                 630                 635                 640

Gln Asp Val Phe Thr Phe Tyr Val Lys Glu Asn Leu Gln Pro Asn Ser
                645                 650                 655
```

Pro Val Gly Met Val Thr Val Met Asp Ala Asp Lys Gly Arg Asn Ala
660 665 670

Glu Met Ser Leu Tyr Ile Glu Glu Asn Asn Asn Ile Phe Ser Ile Glu
675 680 685

Asn Asp Thr Gly Thr Ile Tyr Ser Thr Met Ser Phe Asp Arg Glu His
690 695 700

Gln Thr Thr Tyr Thr Phe Arg Val Lys Ala Val Asp Gly Gly Asp Pro
705 710 715 720

Pro Arg Ser Ala Thr Ala Thr Val Ser Leu Phe Val Met Asp Glu Asn
725 730 735

Asp Asn Ala Pro Thr Val Thr Leu Pro Lys Asn Ile Ser Tyr Thr Leu
740 745 750

Leu Pro Pro Ser Ser Asn Val Arg Thr Val Val Ala Thr Val Leu Ala
755 760 765

Thr Asp Ser Asp Asp Gly Ile Asn Ala Asp Leu Asn Tyr Ser Ile Val
770 775 780

Gly Gly Asn Pro Phe Lys Leu Phe Glu Ile Asp Pro Thr Ser Gly Val
785 790 795 800

Val Ser Leu Val Gly Lys Leu Thr Gln Lys His Tyr Gly Leu His Arg
805 810 815

Leu Val Val Gln Val Asn Asp Ser Gly Gln Pro Ser Gln Ser Thr Thr
820 825 830

Thr Val Val His Val Phe Val Asn Glu Ser Val Ser Asn Ala Thr Ala
835 840 845

Ile Asp Ser Gln Ile Ala Arg Ser Leu His Ile Pro Leu Thr Gln Asp
850 855 860

Ile Ala Gly Asp Pro Ser Tyr Glu Ile Ser Lys Gln Arg Leu Ser Ile
865 870 875 880

Val Ile Gly Val Val Ala Gly Ile Met Thr Val Ile Leu Ile Ile Leu
885 890 895

Ile Val Val Met Ala Arg Tyr Cys Arg Ser Lys Asn Lys Asn Gly Tyr
900 905 910

Glu Ala Gly Lys Lys Asp His Glu Asp Phe Phe Thr Pro Gln Gln His
915 920 925

Asp Lys Ser Lys Lys Pro Lys Lys Asp Lys Lys Asn Lys Lys Ser Lys
930 935 940

Gln Pro Leu Tyr Ser Ser Ile Val Thr Val Glu Ala Ser Lys Pro Asn
945 950 955 960

Gly Gln Arg Tyr Asp Ser Val Asn Glu Lys Leu Ser Asp Ser Pro Ser

965 970 975

Met Gly Arg Tyr Arg Ser Val Asn Gly Gly Pro Gly Ser Pro Asp Leu
980 985 990

Ala Arg His Tyr Lys Ser Ser Ser Pro Leu Pro Thr Val Gln Leu His
995 1000 1005

Pro Gln Ser Pro Thr Ala Gly Lys Lys His Gln Ala Val Gln Asp
1010 1015 1020

Leu Pro Pro Ala Asn Thr Phe Val Gly Ala Gly Asp Asn Ile Ser
1025 1030 1035

Ile Gly Ser Asp His Cys Ser Glu Tyr Ser Cys Gln Thr Asn Asn
1040 1045 1050

Lys Tyr Ser Lys Gln Met Arg Leu His Pro Tyr Ile Thr Val Phe
1055 1060 1065

Gly

<210> 205
<211> 401
<212> PRT
<213> Homo sapiens

<400> 205

Met Ser Phe Ser Lys Thr His Ser Thr Ala Thr Met Pro Pro Pro Ile
1 5 10 15

Asn Pro Ile Leu Ala Ser Leu Gln His Asn Ser Ile Leu Thr Pro Thr
20 25 30

Arg Val Ser Ser Ser Ala Thr Lys Gln Lys Val Leu Ser Pro Pro His
35 40 45

Ile Lys Ala Asp Phe Asn Leu Ala Asp Phe Glu Cys Glu Glu Asp Pro
50 55 60

Phe Asp Asn Leu Glu Leu Lys Thr Ile Asp Glu Lys Glu Glu Leu Arg
65 70 75 80

Asn Ile Leu Val Gly Thr Thr Gly Pro Ile Met Ala Gln Leu Leu Asp
85 90 95

Asn Asn Leu Pro Arg Gly Gly Ser Gly Ser Val Leu Gln Asp Glu Glu
100 105 110

Val Leu Ala Ser Leu Glu Arg Ala Thr Leu Asp Phe Lys Pro Leu His
115 120 125

Lys Pro Asn Gly Phe Ile Thr Leu Pro Gln Leu Gly Asn Cys Glu Lys
130 135 140

Met Ser Leu Ser Ser Lys Val Ser Leu Pro Pro Ile Pro Ala Val Ser
145 150 155 160

Asn Ile Lys Ser Leu Ser Phe Pro Lys Leu Asp Ser Asp Asp Ser Asn

165 170 175

Gln Lys Thr Ala Lys Leu Ala Ser Thr Phe His Ser Thr Ser Cys Leu
180 185 190

Arg Asn Gly Thr Phe Gln Asn Ser Leu Lys Pro Ser Thr Gln Ser Ser
195 200 205

Ala Ser Glu Leu Asn Gly His His Thr Leu Gly Leu Ser Ala Leu Asn
210 215 220

Leu Asp Ser Gly Thr Glu Met Pro Ala Leu Thr Ser Ser Gln Met Pro
225 230 235 240

Ser Leu Ser Val Leu Ser Val Cys Thr Glu Glu Ser Ser Pro Pro Asn
245 250 255

Thr Gly Pro Thr Val Thr Pro Pro Asn Phe Ser Val Ser Gln Val Pro
260 265 270

Asn Met Pro Ser Cys Pro Gln Ala Tyr Ser Glu Leu Gln Met Leu Ser
275 280 285

Pro Ser Glu Arg Gln Cys Val Glu Thr Val Val Asn Met Gly Tyr Ser
290 295 300

Tyr Glu Cys Val Leu Arg Ala Met Lys Lys Lys Gly Glu Asn Ile Glu
305 310 315 320

Gln Ile Leu Asp Tyr Leu Phe Ala His Gly Gln Leu Cys Glu Lys Gly
325 330 335

Phe Asp Pro Leu Leu Val Glu Glu Ala Leu Glu Met His Gln Cys Ser
340 345 350

Glu Glu Lys Met Met Glu Phe Leu Gln Leu Met Ser Lys Phe Lys Glu
355 360 365

Met Gly Phe Glu Leu Lys Asp Ile Lys Glu Val Leu Leu Leu His Asn
370 375 380

Asn Asp Gln Asp Asn Ala Leu Glu Asp Leu Met Ala Arg Ala Gly Ala
385 390 395 400

Ser

<210> 206
<211> 285
<212> PRT
<213> Homo sapiens

<400> 206

Met Glu Val Pro Pro Pro Asp Ala Gly Ser Phe Leu Cys Arg Ala Leu
1 5 10 15

Cys Leu Phe Pro Arg Val Phe Ala Ala Glu Ala Val Thr Ala Asp Ser
20 25 30

Glu Val Leu Glu Glu Arg Gln Lys Arg Leu Pro Tyr Val Pro Glu Pro

35 40 45

Tyr Tyr Pro Glu Ser Gly Trp Asp Arg Leu Arg Glu Leu Phe Gly Lys
50 55 60

Asp Glu Gln Gln Arg Ile Ser Lys Asp Leu Ala Asn Ile Cys Lys Thr
65 70 75 80

Ala Ala Thr Ala Gly Ile Ile Gly Trp Val Tyr Gly Gly Ile Pro Ala
85 90 95

Phe Ile His Ala Lys Gln Gln Tyr Ile Glu Gln Ser Gln Ala Glu Ile
100 105 110

Tyr His Asn Arg Phe Asp Ala Val Gln Ser Ala His Arg Ala Ala Thr
115 120 125

Arg Gly Phe Ile Arg Tyr Gly Trp Arg Trp Gly Trp Arg Thr Ala Val
130 135 140

Phe Val Thr Ile Phe Asn Thr Val Asn Thr Ser Leu Asn Val Tyr Arg
145 150 155 160

Asn Lys Asp Ala Leu Ser His Phe Val Ile Ala Gly Ala Val Thr Gly
165 170 175

Ser Leu Phe Arg Ile Asn Val Gly Leu Arg Gly Leu Val Ala Gly Gly
180 185 190

Ile Ile Gly Ala Leu Leu Gly Thr Pro Val Gly Gly Leu Leu Met Ala
195 200 205

Phe Gln Lys Tyr Ser Gly Glu Thr Val Gln Glu Arg Lys Gln Lys Asp
210 215 220

Arg Lys Ala Leu His Glu Leu Lys Leu Glu Glu Trp Lys Gly Arg Leu
225 230 235 240

Gln Val Thr Glu His Leu Pro Glu Lys Ile Glu Ser Ser Leu Gln Glu
245 250 255

Asp Glu Pro Glu Asn Asp Ala Lys Lys Ile Glu Ala Leu Leu Asn Leu
260 265 270

Pro Arg Asn Pro Ser Val Ile Asp Lys Gln Asp Lys Asp
275 280 285

<210> 207
<211> 212
<212> PRT
<213> Homo sapiens

<400> 207

Met Leu Asn Lys Val Leu Ser Arg Leu Gly Val Ala Gly Gln Trp Arg
1 5 10 15

Phe Val Asp Val Leu Gly Leu Glu Glu Glu Ser Leu Gly Ser Val Pro
20 25 30

Ala Pro Ala Cys Ala Leu Leu Leu Leu Leu Phe Pro Leu Thr Ala Gln His

```
        35                  40                  45

Glu Asn Phe Arg Lys Lys Gln Ile Glu Glu Leu Lys Gly Gln Glu Val
    50                  55                  60

Ser Pro Lys Val Tyr Phe Met Lys Gln Thr Ile Gly Asn Ser Cys Gly
65                  70                  75                  80

Thr Ile Gly Leu Ile His Ala Val Ala Asn Asn Gln Asp Lys Leu Gly
                85                  90                  95

Phe Glu Asp Gly Ser Val Leu Lys Gln Phe Leu Ser Glu Thr Glu Lys
            100                 105                 110

Met Ser Pro Glu Asp Arg Ala Lys Cys Phe Glu Lys Asn Glu Ala Ile
        115                 120                 125

Gln Ala Ala His Asp Ala Val Ala Gln Glu Gly Gln Cys Arg Val Asp
    130                 135                 140

Asp Lys Val Asn Phe His Phe Ile Leu Phe Asn Asn Val Asp Gly His
145                 150                 155                 160

Leu Tyr Glu Leu Asp Gly Arg Met Pro Phe Pro Val Asn His Gly Ala
                165                 170                 175

Ser Ser Glu Asp Thr Leu Leu Lys Asp Ala Ala Lys Val Cys Arg Glu
            180                 185                 190

Phe Thr Glu Arg Glu Gln Gly Glu Val Arg Phe Ser Ala Val Ala Leu
        195                 200                 205

Cys Lys Ala Ala
    210
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<210> 208
<211> 596
<212> PRT
<213> Homo sapiens

<400> 208

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Met Ser Leu Ser Met Arg Asp Pro Val Ile Pro Gly Thr Ser Met Ala
1               5                   10                  15

Tyr His Pro Phe Leu Pro His Arg Ala Pro Asp Phe Ala Met Ser Ala
            20                  25                  30

Val Leu Gly His Gln Pro Pro Phe Phe Pro Ala Leu Thr Leu Pro Pro
        35                  40                  45

Asn Gly Ala Ala Ala Leu Ser Leu Pro Gly Ala Leu Ala Lys Pro Ile
    50                  55                  60

Met Asp Gln Leu Val Gly Ala Ala Glu Thr Gly Ile Pro Phe Ser Ser
65                  70                  75                  80

Leu Gly Pro Gln Ala His Leu Arg Pro Leu Lys Thr Met Glu Pro Glu
                85                  90                  95

Glu Glu Val Glu Asp Asp Pro Lys Val His Leu Glu Ala Lys Glu Leu
```



```
            100                 105                 110

Trp Asp Gln Phe His Lys Arg Gly Thr Glu Met Val Ile Thr Lys Ser
        115                 120                 125

Gly Arg Arg Met Phe Pro Pro Phe Lys Val Arg Cys Ser Gly Leu Asp
    130                 135                 140

Lys Lys Ala Lys Tyr Ile Leu Leu Met Asp Ile Ile Ala Ala Asp Asp
145                 150                 155                 160

Cys Arg Tyr Lys Phe His Asn Ser Arg Trp Met Val Ala Gly Lys Ala
                165                 170                 175

Asp Pro Glu Met Pro Lys Arg Met Tyr Ile His Pro Asp Ser Pro Ala
            180                 185                 190

Thr Gly Glu Gln Trp Met Ser Lys Val Val Thr Phe His Lys Leu Lys
        195                 200                 205

Leu Thr Asn Asn Ile Ser Asp Lys His Gly Phe Thr Leu Ala Phe Pro
    210                 215                 220

Ser Asp His Ala Thr Trp Gln Gly Asn Tyr Ser Phe Gly Thr Gln Thr
225                 230                 235                 240

Ile Leu Asn Ser Met His Lys Tyr Gln Pro Arg Phe His Ile Val Arg
                245                 250                 255

Ala Asn Asp Ile Leu Lys Leu Pro Tyr Ser Thr Phe Arg Thr Tyr Leu
            260                 265                 270

Phe Pro Glu Thr Glu Phe Ile Ala Val Thr Ala Tyr Gln Asn Asp Lys
        275                 280                 285

Ile Thr Gln Leu Lys Ile Asp Asn Asn Pro Phe Ala Lys Gly Phe Arg
    290                 295                 300

Asp Thr Gly Asn Gly Arg Arg Glu Lys Arg Gln Gln Leu Thr Leu Gln
305                 310                 315                 320

Ser Met Arg Val Phe Asp Glu Arg His Lys Lys Glu Asn Gly Thr Ser
                325                 330                 335

Asp Glu Ser Ser Ser Glu Gln Ala Ala Phe Asn Cys Phe Ala Gln Ala
            340                 345                 350

Ser Ser Pro Ala Ala Ser Thr Val Gly Thr Ser Asn Leu Lys Asp Leu
        355                 360                 365

Cys Pro Ser Glu Gly Glu Ser Asp Ala Glu Ala Glu Ser Lys Glu Glu
    370                 375                 380

His Gly Pro Glu Ala Cys Asp Ala Ala Lys Ile Ser Thr Thr Thr Ser
385                 390                 395                 400

Glu Glu Pro Cys Arg Asp Lys Gly Ser Pro Ala Val Lys Ala His Leu
                405                 410                 415
```

```
Phe Ala Ala Glu Arg Pro Arg Asp Ser Gly Arg Leu Asp Lys Ala Ser
            420                 425                 430

Pro Asp Ser Arg His Ser Pro Ala Thr Ile Ser Ser Ser Thr Arg Gly
        435                 440                 445

Leu Gly Ala Glu Glu Arg Arg Ser Pro Val Arg Glu Gly Thr Ala Pro
    450                 455                 460

Ala Lys Val Glu Glu Ala Arg Ala Leu Pro Gly Lys Glu Ala Phe Ala
465                 470                 475                 480

Pro Leu Thr Val Gln Thr Asp Ala Ala Arg Ser Ser Val His Arg His
                485                 490                 495

Pro Phe Arg Asn Leu Asn Thr Met Arg Pro Arg Leu Arg Tyr Ser Pro
            500                 505                 510

Tyr Ser Ile Pro Val Pro Val Pro Asp Gly Ser Ser Leu Leu Thr Thr
        515                 520                 525

Ala Leu Ala Ala Ser Pro Ala Ser Val Ala Val Asp Ser Gly Ser Glu
    530                 535                 540

Leu Asn Ser Arg Ser Ser Thr Leu Ser Ser Ser Ser Met Ser Leu Ser
545                 550                 555                 560

Pro Lys Leu Cys Ala Glu Lys Glu Ala Ala Thr Ser Glu Leu Gln Ser
                565                 570                 575

Ile Gln Arg Leu Val Ser Gly Leu Glu Ala Lys Pro Asp Arg Ser Arg
            580                 585                 590

Ser Ala Ser Pro
        595
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<210> 209
<211> 215
<212> PRT
<213> Homo sapiens

<400> 209

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Met Gly Lys Gly Asp Pro Lys Lys Pro Arg Gly Lys Met Ser Ser Tyr
1               5                   10                  15

Ala Phe Phe Val Gln Thr Cys Arg Glu Glu His Lys Lys Lys His Pro
            20                  25                  30

Asp Ala Ser Val Asn Phe Ser Glu Phe Ser Lys Lys Cys Ser Glu Arg
        35                  40                  45

Trp Lys Thr Met Ser Ala Lys Glu Lys Gly Lys Phe Glu Asp Met Ala
    50                  55                  60

Lys Ala Asp Lys Ala Arg Tyr Glu Arg Glu Met Lys Thr Tyr Ile Pro
65                  70                  75                  80

Pro Lys Gly Glu Thr Lys Lys Lys Phe Lys Asp Pro Asn Ala Pro Lys
                85                  90                  95
```



```
Arg Pro Pro Ser Ala Phe Phe Leu Phe Cys Ser Glu Tyr Arg Pro Lys
            100                 105                 110

Ile Lys Gly Glu His Pro Gly Leu Ser Ile Gly Asp Val Ala Lys Lys
        115                 120                 125

Leu Gly Glu Met Trp Asn Asn Thr Ala Ala Asp Asp Lys Gln Pro Tyr
    130                 135                 140

Glu Lys Lys Ala Ala Lys Leu Lys Glu Lys Tyr Glu Lys Asp Ile Ala
145                 150                 155                 160

Ala Tyr Arg Ala Lys Gly Lys Pro Asp Ala Ala Lys Lys Gly Val Val
                165                 170                 175

Lys Ala Glu Lys Ser Lys Lys Lys Lys Glu Glu Glu Glu Asp Glu Glu
            180                 185                 190

Asp Glu Glu Asp Glu Glu Glu Glu Glu Asp Glu Glu Asp Glu Asp Glu
        195                 200                 205

Glu Glu Asp Asp Asp Asp Glu
    210                 215
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<210> 210
<211> 243
<212> PRT
<213> Homo sapiens

<400> 210

```
Met Ala Ala Ile Ala Ala Ser Glu Val Leu Val Asp Ser Ala Glu Glu
1               5                   10                  15

Gly Ser Leu Ala Ala Ala Ala Glu Leu Ala Ala Gln Lys Arg Glu Gln
            20                  25                  30

Arg Leu Arg Lys Phe Arg Glu Leu His Leu Met Arg Asn Glu Ala Arg
        35                  40                  45

Lys Leu Asn His Gln Glu Val Val Glu Glu Asp Lys Arg Leu Lys Leu
    50                  55                  60

Pro Ala Asn Trp Glu Ala Lys Lys Ala Arg Leu Glu Trp Glu Leu Lys
65                  70                  75                  80

Glu Glu Glu Lys Lys Lys Glu Cys Ala Ala Arg Gly Glu Asp Tyr Glu
                85                  90                  95

Lys Val Lys Leu Leu Glu Ile Ser Ala Glu Asp Ala Glu Arg Trp Glu
            100                 105                 110

Arg Lys Lys Lys Arg Lys Asn Pro Asp Leu Gly Phe Ser Asp Tyr Ala
        115                 120                 125

Ala Ala Gln Leu Arg Gln Tyr His Arg Leu Thr Lys Gln Ile Lys Pro
    130                 135                 140

Asp Met Glu Thr Tyr Glu Arg Leu Arg Glu Lys His Gly Glu Glu Phe
145                 150                 155                 160
```

```
Phe Pro Thr Ser Asn Ser Leu Leu His Gly Thr His Val Pro Ser Thr
                165                 170                 175

Glu Glu Ile Asp Arg Met Val Ile Asp Leu Glu Lys Gln Ile Glu Lys
            180                 185                 190

Arg Asp Lys Tyr Ser Arg Arg Arg Pro Tyr Asn Asp Asp Ala Asp Ile
        195                 200                 205

Asp Tyr Ile Asn Glu Arg Asn Ala Lys Phe Asn Lys Lys Ala Glu Arg
    210                 215                 220

Phe Tyr Gly Lys Tyr Thr Ala Glu Ile Lys Gln Asn Leu Glu Arg Gly
225                 230                 235                 240

Thr Ala Val
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<210> 211
<211> 479
<212> PRT
<213> Homo sapiens

<400> 211

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Met Leu Gln Ile Asn Gln Met Phe Ser Val Gln Leu Ser Leu Gly Glu
1               5                   10                  15

Gln Thr Trp Glu Ser Glu Gly Ser Ser Ile Lys Lys Ala Gln Gln Ala
            20                  25                  30

Val Ala Asn Lys Ala Leu Thr Glu Ser Thr Leu Pro Lys Pro Val Gln
        35                  40                  45

Lys Pro Pro Lys Ser Asn Val Asn Asn Asn Pro Gly Ser Ile Thr Pro
    50                  55                  60

Thr Val Glu Leu Asn Gly Leu Ala Met Lys Arg Gly Glu Pro Ala Ile
65                  70                  75                  80

Tyr Arg Pro Leu Asp Pro Lys Pro Phe Pro Asn Tyr Arg Ala Asn Tyr
                85                  90                  95

Asn Phe Arg Gly Met Tyr Asn Gln Arg Tyr His Cys Pro Val Pro Lys
            100                 105                 110

Ile Phe Tyr Val Gln Leu Thr Val Gly Asn Asn Glu Phe Phe Gly Glu
        115                 120                 125

Gly Lys Thr Arg Gln Ala Ala Arg His Asn Ala Ala Met Lys Ala Leu
    130                 135                 140

Gln Ala Leu Gln Asn Glu Pro Ile Pro Glu Arg Ser Pro Gln Asn Gly
145                 150                 155                 160

Glu Ser Gly Lys Asp Met Asp Asp Asp Lys Asp Ala Asn Lys Ser Glu
                165                 170                 175

Ile Ser Leu Val Phe Glu Ile Ala Leu Lys Arg Asn Met Pro Val Ser
            180                 185                 190
```



```
Phe Glu Val Ile Lys Glu Ser Gly Pro Pro His Met Lys Ser Phe Val
        195                 200                 205

Thr Arg Val Ser Val Gly Glu Phe Ser Ala Glu Gly Glu Gly Asn Ser
    210                 215                 220

Lys Lys Leu Ser Lys Lys Arg Ala Ala Thr Thr Val Leu Gln Glu Leu
225                 230                 235                 240

Lys Lys Leu Pro Pro Leu Pro Val Val Glu Lys Pro Lys Leu Phe Phe
                245                 250                 255

Lys Lys Arg Pro Lys Thr Ile Val Lys Ala Gly Pro Glu Tyr Gly Gln
            260                 265                 270

Gly Met Asn Pro Ile Ser Arg Leu Ala Gln Ile Gln Gln Ala Lys Lys
        275                 280                 285

Glu Lys Glu Pro Asp Tyr Val Leu Leu Ser Glu Arg Gly Met Pro Arg
    290                 295                 300

Arg Arg Glu Phe Val Met Gln Val Lys Val Gly Asn Glu Val Ala Thr
305                 310                 315                 320

Gly Thr Gly Pro Asn Lys Lys Ile Ala Lys Lys Asn Ala Ala Glu Ala
                325                 330                 335

Met Leu Leu Gln Leu Gly Tyr Lys Ala Ser Thr Asn Leu Gln Asp Gln
            340                 345                 350

Leu Glu Lys Thr Gly Glu Asn Lys Gly Trp Ser Gly Pro Lys Pro Gly
        355                 360                 365

Phe Pro Glu Pro Thr Asn Asn Thr Pro Lys Gly Ile Leu His Leu Ser
    370                 375                 380

Pro Asp Val Tyr Gln Glu Met Glu Ala Ser Arg His Lys Val Ile Ser
385                 390                 395                 400

Gly Thr Thr Leu Gly Tyr Leu Ser Pro Lys Asp Met Asn Gln Pro Ser
                405                 410                 415

Ser Ser Phe Phe Ser Ile Ser Pro Thr Ser Asn Ser Ser Ala Thr Ile
            420                 425                 430

Ala Arg Glu Leu Leu Met Asn Gly Thr Ser Ser Thr Ala Glu Ala Ile
        435                 440                 445

Gly Leu Lys Gly Ser Ser Pro Thr Pro Pro Cys Ser Pro Val Gln Pro
    450                 455                 460

Ser Lys Gln Leu Glu Tyr Leu Ala Arg Ile Gln Gly Phe Gln Val
465                 470                 475
```

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December 17, 2004

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COPY

Our Ref.: P03-0038US

Please file this application Before December 26, 2004

Re : New National Phase Application in U.S.A. derived from PCT/JP2003/008036
in the name of TAKEDA PHARMACEUTICAL COMPANY LIMITED

Dear Sirs:

Please proceed with the national entry from the above-identified PCT international application before a 30-month deadline of December 26, 2004.

Please refer to the Additional Instructions and Filing Particulars Sheet. If anything further is required for the national entry, please so inform us immediately.

We thank you for your cooperation with this new case and kindly ask you to acknowledge safe receipt of this letter by return facsimile.

Sincerely yours,
ABE, IKUBO & KATAYAMA

Hiroshi Kobayashi
Patent Attorney

Encls.: Additional Instructions
Filing Particular Sheet

HK/tw

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End of Text.

Regarding the references for IDS, we send you hard copies (15 – 21).

Filing Particulars

Takeda's Case No. 3060US0P,EP0W
Our Ref: P03-0038US,EP

(1) Title of the Invention
Preventing/Treating Agent for Cancer

(2) Applicant
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(4) Pct International Application
Application No. PCT/JP2003/008036
Filing Date: June 25, 2003

(5) Japanese Patent Application(s) from which the present application claims priority

Country	Date of Filing	Application No.	Priority
a) Japan	June 26, 2002	186799/2002	yes
b) Japan	June 26, 2002	186815/2002	yes

a) Applicant: The same as above (2)
Inventors: (A) , (B) and (C)
b) Applicant: The same as above (2)
Inventors: (A) and (B)